1994

Studies of Silica as a Polymer Support for Regioselective Reactions on Sucrose

Lei Cheng

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STUDIES OF SILICA AS A POLYMER SUPPORT FOR

REGIOSELECTIVE REACTIONS ON SUCROSE

(TITLE)

BY

Lei Cheng

THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF

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YEAR

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STUDIES OF SILICA AS A POLYMER SUPPORT FOR REGIOSELECTIVE REACTIONS ON SUCROSE

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Lei Cheng

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Date

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ABSTRACT

Sucrose is a material that has potential for replacing oil as an industrial feedstock, at least in some instances. A major difficulty in utilizing sucrose is the lack of regioselectivity in its reactions due to the many reactive sites on the sucrose molecule.

This research is part of an attempt to study the technique of molecular recognition in an effort to increase reaction regioselectivity. Molecular recognition by template imprinting should be a way to create a material that would "recognize" and bind to sucrose in such a way as to block certain of the hydroxyl groups on the sucrose. The strategy in this research is to use D-glucose as a template to synthesize a monomer with covalently bonded vinyl groups. The monomer would then be copolymerized with another monomer and a crosslinking agent to prepare a three dimensional polymer, incorporating the glucose template. Removal of the glucose would leave a cavity with the same stereochemical features as the glucose part of the sucrose molecule. Sucrose should then bind to the polymer cavity. The stereo location of the functional groups inside the cavity would be primarily responsible for the molecular recognition characteristics of the cavity. This method could increase the regioselectivity of some reactions of sucrose by blocking the glucose end of sucrose to permit reactions to occur on the fructose portion. Alternatively, a reaction might occur within the cavity.

Methyl 3-O-vinylbenzyl-2,4,6-tri-O-methacroyl-α-D-glucopyranoside was chosen as a possible monomer to demonstrate the execution of a regioselective reaction on the 3 position of the glucose within the polymer cavity. A partial

syntheses of this monomer has been completed.

The surface of wide pore silica was coated with a fifty angstrom thick layer of the polymer described above. Studies of the cavities obtained and further investigation using HPLC and other techniques are continuing.

DEDICATION

To my advisor, Professor Jerry W. Ellis, for his tremendous contribution in providing me guidance, inspiration, and assistance.

ACKNOWLEDGEMENT

I would like to thank my advisor, Dr. Jerry W. Ellis, for the professional help and suggestions during this work.

I would also like to thank the other professors and staff, especially Matt and Ken, (stockroom staff of the chemistry department) and the other members of our research group, for their assistance.

The work described in this thesis was made possible through donations from The Sugar Association, along with financial support from Eastern Illinois University.

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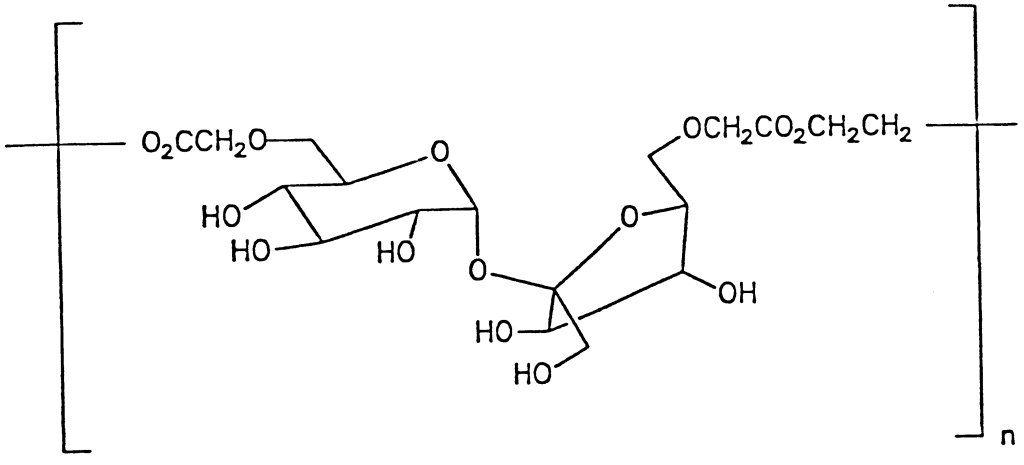
CHAPTER 1

INTRODUCTION

A. Background

Modern industrial feedstocks are critically dependent upon oil which is a non-renewable material. Eventually we will be totally dependent upon renewable natural resources for most of our products. Sucrose is produced from sugar beets and sugar cane which can be grown over a variety of climates and the current world production of sucrose is about one hundred and ten million tons per year. With current refining technologies sucrose can be produced inexpensively and in high purity. The use of sucrose as an industrial renewable material has tremendous possibilities. The relatively unstable glycosidic linkage would suggest that a biodegradable polymer might be formed from sucrose. Crosslinked polymers of



A Possible Linear Polymer of Sucrose.
Figure 1

sucrose are easily prepared, but a linear polymer, such as the one shown in Figure 1, would be more versatile.

A major difficulty in utilizing sucrose as a feedstock is the lack of regioselectivity in synthetic reactions due to the many reactive sites on the molecule. Since the sucrose molecule contains three primary and five secondary hydroxyl groups, many products can be produced.[1] It can form eight possible monosubstitution products, twenty-eight possible disubstitution products, etc., so the typical reaction results in a very complex mixture requiring difficult separations in order to isolate a particular product in pure form. With so many products formed, the yield of any one of these is quite low. For example, direct acylation of sucrose with acid chlorides[2,3] leads to mixture of mono-, di- and tri-esters which are difficult to separate. Transesterification, using either natural triglycerides or methyl esters of fatty acids, also leads to mixtures.[4] Regioselective monoacylation of mono- and disaccharides can be effected when sophisticated acylation agents such as special amides or thioesters are used in the presence of NaH in pyridine.[5,6]

For those industrial or commercial applications where a mixture is acceptable, regioselectivity is not important. But clearly, the lack of regioselectivity is an important limitation to the further exploitation of sucrose as an important industrial feedstock.

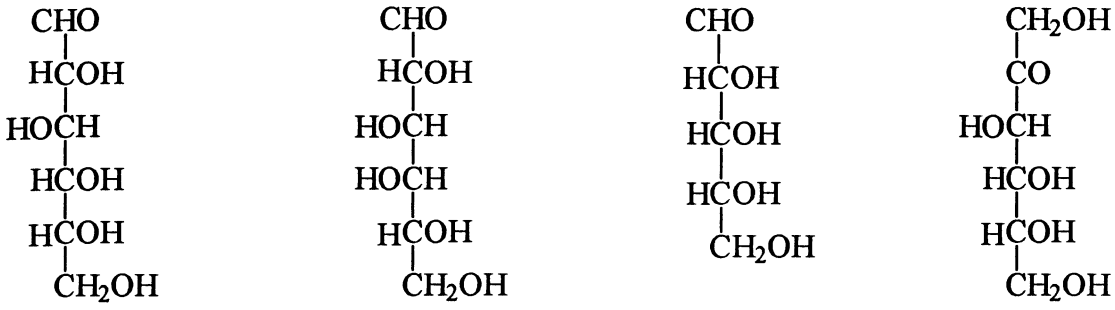
The technique referred to as molecular recognition might be used to increase the regioselectivity of some reactions of sucrose. Molecular recognition by template

imprinting might lead to the production of a reusable material that would "recognize" and bind to sucrose in such a way as to block certain of the hydroxyl groups. This approach would utilize the combination of molecular recognition and solid phase synthesis to possibly bring about a regioselective reaction on sucrose. For example, a cavity might be produced, into which only the glucose end of sucrose could enter. Waiting inside at the 4 or 6 position would be a site for a transesterification reaction, the product of which might be a mono-acetate of sucrose. This process could be analogous to that of an enzyme and is currently considered a viable possibility.[7] The long range goal of this research is to demonstrate the concept of molecular recognition on the sucrose molecule.

B. Carbohydrates

Carbohydrates are a diverse group of substances of broad biochemical significance. The most general way of describing these compounds, which is satisfactory in nearly all situations, is that carbohydrates are polyhydroxy aldehydes and ketones, and the polymers derived from these compounds.[8] Simple sugars are called monosaccharides and two monosaccharides bonded by a glycosidic linkage are called disaccharides. Larger such combinations are oligosaccharides and polysaccharides.[9]

These compounds also are known as aldoses and ketoses. Common aldohexoses (six carbon) include D-glucose (**1**), D-galactose (**2**), and D-ribose (**3**) while D-fructose (**4**) is the most common ketohexose; these structures are shown in Figure 2. The aldohexoses contain four chiral centers and have sixteen possible stereoisomers, so eight pairs of enantiomers are expected. All sixteen of these possible stereoisomers are now known, although only three, (D)-glucose, (D)-mannose, and (D)-galactose, are found in abundance. Glucose typically exists as a cyclic structure which is an intramolecular hemiacetal. The cyclic form of D-glucose is shown in Figure 3 as a chair conformation and a Haworth projection.

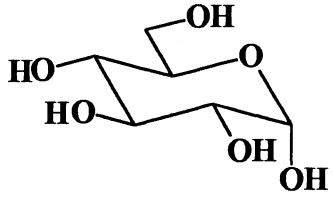


D - glucose **D - galactose** **D - ribose** **D - frutose**

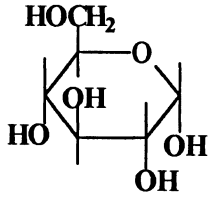
1 **2** **3** **4**

The Structures of Some Common Monosaccharides.

Figure 2



Chair Conformation

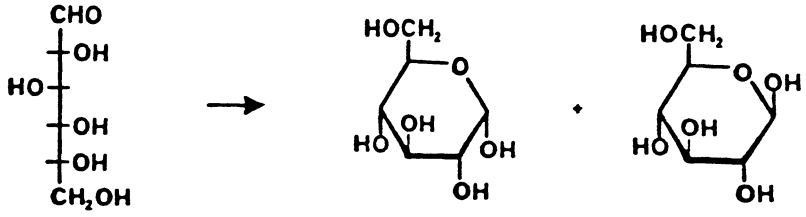


Haworth Projection

The Cyclic Structure of Glucose

Figure 3

Since the formation of a cyclic structure from an acyclic aldose or ketose generates a new chiral center, ring formation produces two new diastereomeric compounds. The Haworth projections of the two diastereomers produced when D-glucose forms a pyranose ring are shown in Scheme 1.



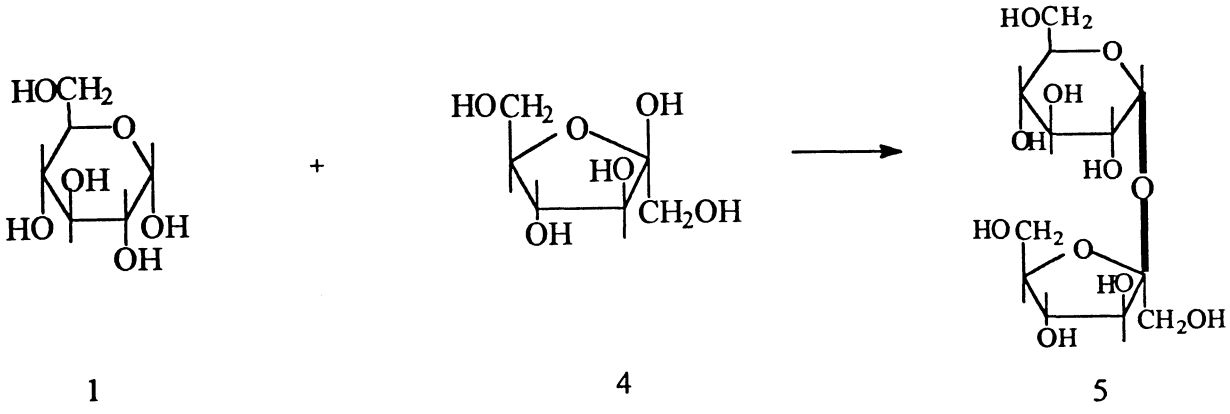
1 α β

The Formation of Diastereomers Through Ring Closing
Scheme 1

These diastereomers are referred to as anomers and are distinguished from each other by the Greek letters α and ß. For a cyclic D-aldose oriented in the standard way, the α anomer has the anomeric hydroxyl group on C-1 projecting below the plane of the ring while the ß anomer has the hydroxyl group directed above the plane of the ring.

When several monosaccharide units are joined together by acetal linkages, oligosaccharides and polysaccharides result. Under proper conditions, hydrolysis of these more complex carbohydrates regenerates the constituent monosaccharides. Oligosaccharides are compounds formed when small numbers (2-10) of

monosaccharides are coupled together. The coupling is of a specific type; a hydroxyl oxygen from one monosaccharide replaces the anomeric hydroxyl of a second to form a disaccharide. A less common example of a glycosidic linkage is where the C-1 hydroxyl group of glucose replaces the anomeric C-2 hydroxyl group of fructose forming sucrose (**5**), as shown in Scheme 2. The glycosidic linkage is shown as a bold bond.



The Sucrose Glycosidic Linkage
Scheme 2

Of the disaccharides, sucrose and lactose are found abundantly in nature. (D)-Sucrose (**5**) has the molecular formula $C_{12}H_{22}O_{11}$ and is a non-reducing sugar since no hemiacetal is present. When it is hydrolyzed by dilute, aqueous acid or in the present of enzymes, it yields equal amounts of D-(+)-glucose and D-(-)-fructose.

Carbohydrates are most frequently protected by conversion into acetals,

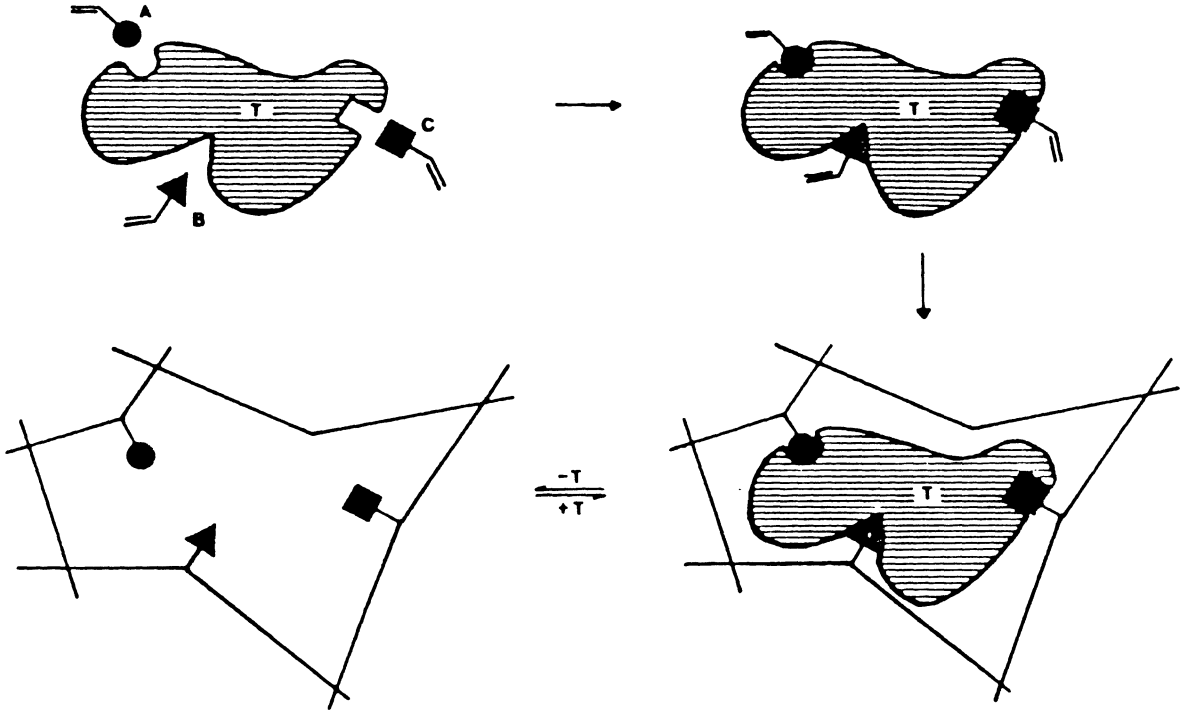
ketals, esters, or ethers. A combination of these protecting groups usually is needed. Esters include acetate, benzoate, carbonate, and nitrate. Ethers typically used are methyl, benzyl, and others. Cyclic acetals include isopropylidene, benzylidene, and methylene. Within each of these four classes of protecting groups, only one or two are generally encountered. For instance, the ketal which most often provides group protection is that derived from acetone. The esters used to protect carbohydrates usually are acetates or benzoates. Acetal and ketal protection to a large extent complements esterification. Esters are moderately stable in the presence of acids but cyclic acetal and ketal protecting groups are not. Acetals and ketals, in contrast, are stable under basic reaction conditions which cause ester removal.

C. Molecular Recognition

The central theme of molecular recognition by template imprinting is to use a specific imprint molecule to coordinate the assembly of polymerizable units around itself. The functional groups to be introduced are bonded to the template molecule in the form of polymerizable vinyl derivatives to form a monomer. This monomer is then copolymerized under such conditions that a highly crosslinked polymer is formed which restricts the chains to a fixed arrangement. After removal of the template, free cavities are formed as shown in Figure 4.

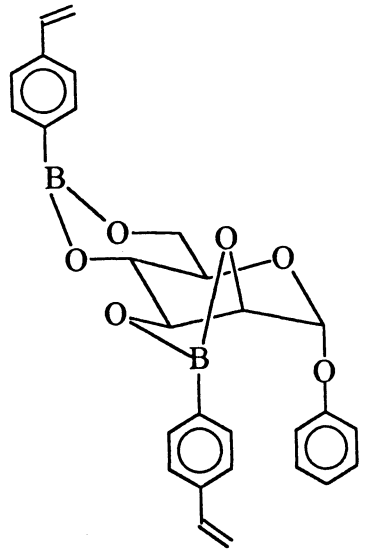
The imprint molecules are removed, leaving a recognition site or cavity complementary to the imprint species in both shape and functionality. The polymer should have a macroporous structure allowing the imprint molecule to diffuse into and out of the cavity. This site constitutes an "induced molecular memory" capable of selectively recognizing the imprint species.

Two essentially different approaches have been developed, covalent and noncovalent. Of the major groups working in the area following the covalent approach, those of Wülff[10,11] in Germany and Shea[12] in California should be mentioned, whereas the noncovalent approach has mainly been developed by Mosbach[13] in Sweden.



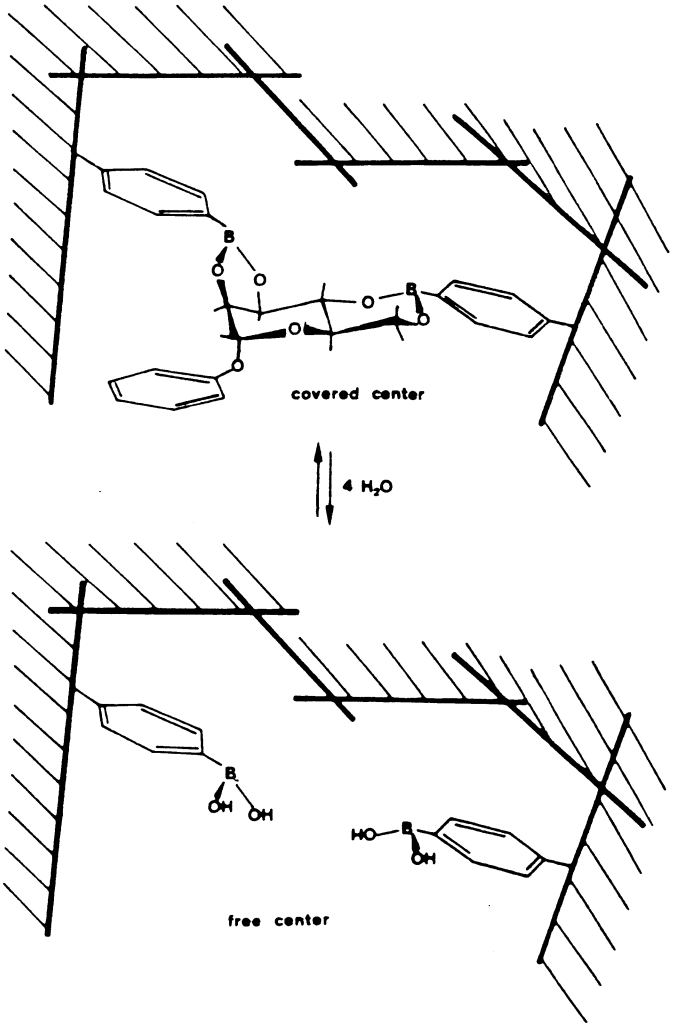
A Schematic Picture of Functional Groups Bonded to a Template Molecule(T), then Locked in Place by a Polymer Framework.[14]
Figure 4

Wülff[14] has used monomer I, (**6**), shown in Figure 5. The template molecule is phenyl α-D-mannopyranoside, to which two molecules of 4-vinylphenylboronic acid are each bound by ester linkages to two hydroxyl groups. This monomer was copolymerized with ethylene glycol dimethacrylate (EGDM), a higher flexibile crosslinking agent. The polymerization conditions used gave macroporous polymers which had a permanent pore structure, high surface area and good accessibility. When this polymer was hydrolyzed with water or methanol, analysis showed that 40 to 90% of the template molecule was removed. This is shown in Figure 6. This hydrolyzed polymer had the ability to resolve the racemate of the template.



6

The Structure of Monomer I (6).[14]
Figure 5



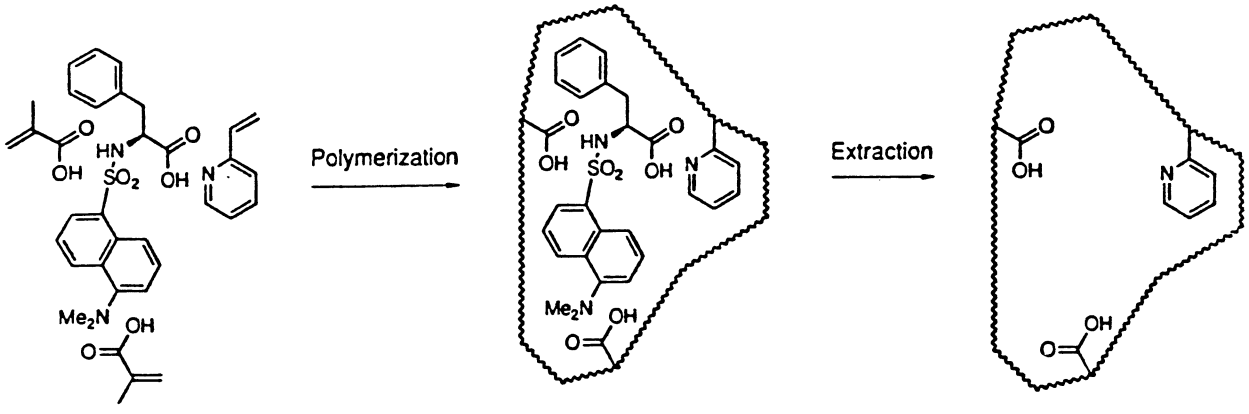
Removal and Uptake of Template.[14]
Figure 6

The evaluation of the selectivity of the polymer cavities prepared by Wülff and others[14] was conducted by testing the ability of the polymer to resolve the racemate of the template. For example, Wülff prepared cavities from D-mannose, exposed the polymer to racemic mannose and analyzed the extent of resolution by optical activity measurements. The results were represented as α, the ratio of the two distribution coefficients between solution and polymer of the L- and D- forms of the template molecule. They found α values between 1.2 to 4.5 for their system.

Mosbach *et al.*[15] prepared dansyl-phenylalanine imprinted polymers using the ion-pair association of template and carboxyl containing monomers in the polymerization step as shown in Figure 7. The functional monomers, methacrylic acid (MAA) and 2-vinylpyridine are arranged around the print molecule, dansyl-L-phenylalanine, as a result of the noncovalent interaction between complementary chemical functionalities. After polymerization, the print molecule is removed by extraction exposing recognition sites possessing a "memory" for the shape and chemical functionality of the print molecule. The selectivity for racemic resolution was good, exhibiting α values of 1.90 to 4.35.

The Goals of This Research

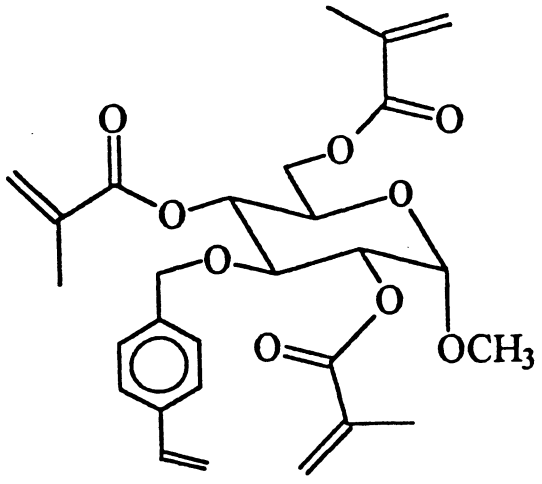
This work was two-fold in purpose. The first was to apply the molecular recognition/template imprinting technique to sucrose, with the polymer on a silica surface to take advantage of the high surface area of silica. The second was to synthesize a new monomer that could possibly demonstrate a chemical reaction within the cavity and thus a regioselective reaction on sucrose.



Schematic Representation of Noncovalent Molecular Imprinting Using an Amino Acid Derivative.[15]
Figure 7

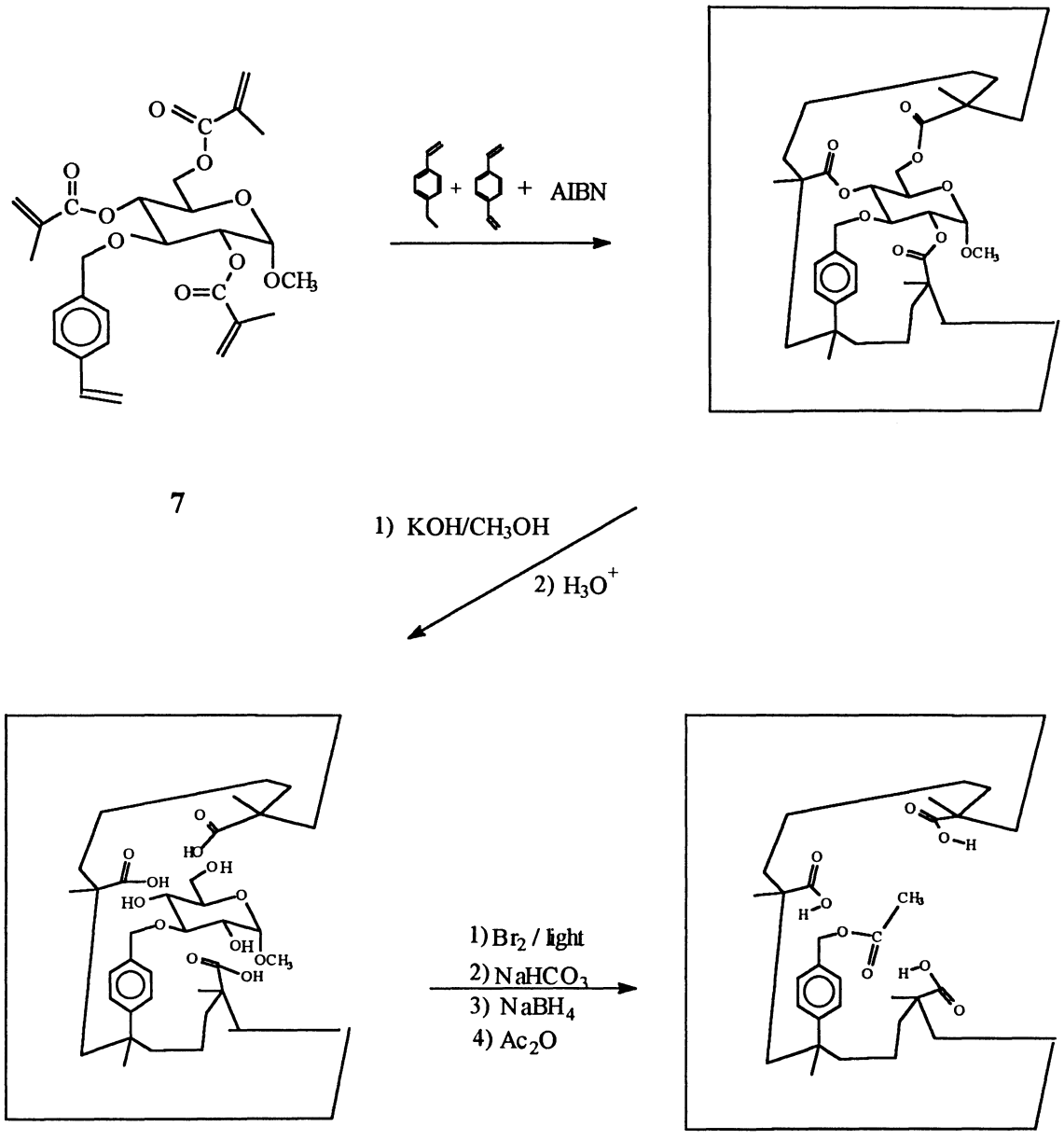
To apply the molecular recognition technology to sucrose, the strategy is to use glucose as a template from which a monomer is synthesized and then polymerized to ultimately create a glucose-specific cavity. The sucrose's glucose part could migrate into the cavity, be positioned and held by hydrogen bonding with the carboxyl group and react with it. Using this concept we could in principle design a cavity for the mono-esterification at any specific site on the glucose (or fructose) end of the sucrose, for example, the 3-monoester. This could be done by using monomer II (**7**), shown in Figure 8, to form the cavity, removing the template by breaking the ester bonds by hydrolysis. The complete release of the template and the conversion of the form ether linkage to the alcohol could all be

done by known chemistry.[16] The conversion of the alcohol into the acetate would provide a cavity that has the acetate situated in just the correct place for transesterification to provide a specific product, the 3-monoacetate of sucrose. All these reactions are shown in Scheme 3. The schematic diagram of sucrose migrating into the cavity, being held by the hydrogen bonding and then by transesterfication, forming a 3-monoacetate is shown in Scheme 4.



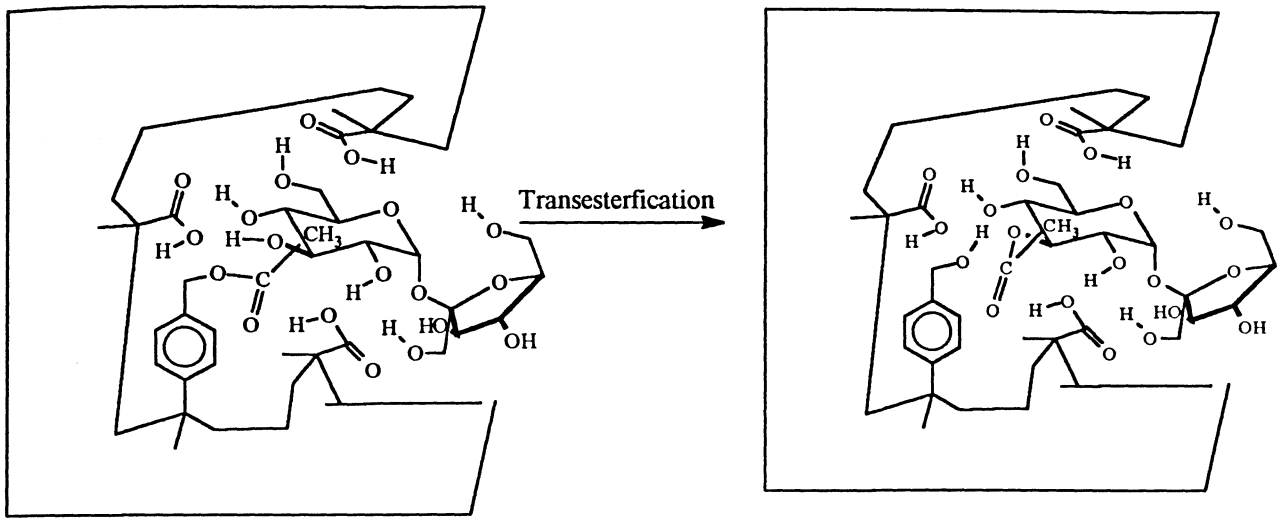
7

The Structure of Monomer II (7).
Figure 8



Schematic Diagram of Cavity Formed by Monomer II (7) with A Functional Transformation in The Cavity

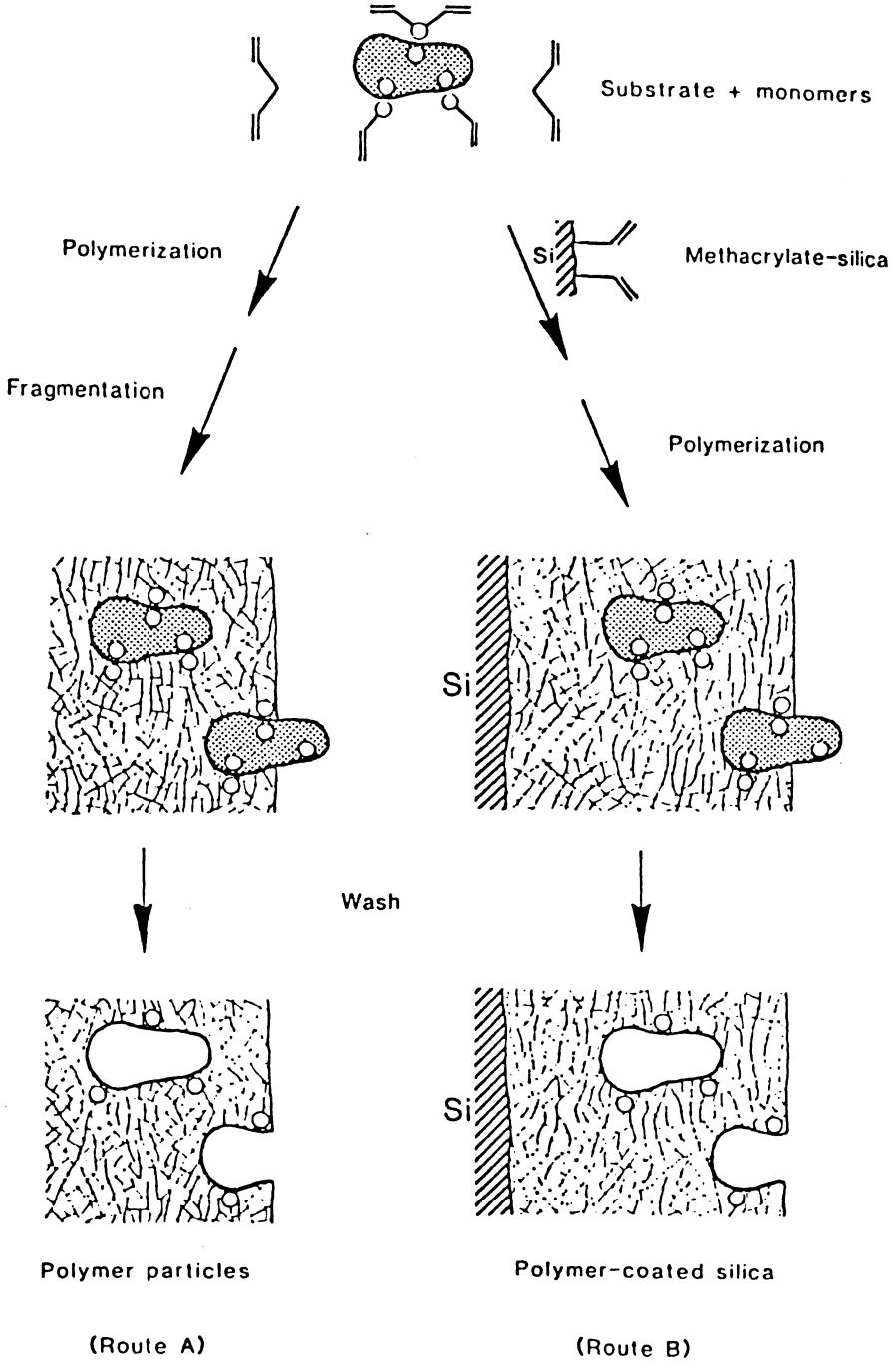
Scheme 3



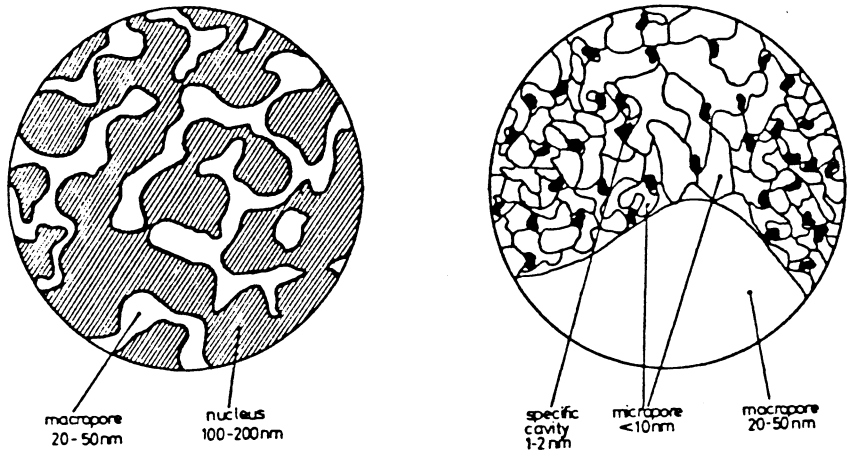
Schematic Picture of The Formation of 3-Mono Acetate of Sucrose
Scheme 4

The Importance of High Surface Area

The polymer formed during this process should have a high surface area to get the desired capacity. The reason is that the greater the surface area, the most likely a cavity will occur at the surface. Those cavities buried inside the polymer matrix would generally be inaccessible to reagents and especially to sucrose. There are two ways to get high surface area polymers; the schematic diagram of these two approaches is shown in Scheme 5. One way is by forming a macroporous polymer (Route A), having high surface area, its structure is shown in Figure 9 and the other way is through polymerization on a surface, such as silica, which already has a high surface area (Route B).



Two Different Approaches To High Surface Areas[41]
Scheme 5



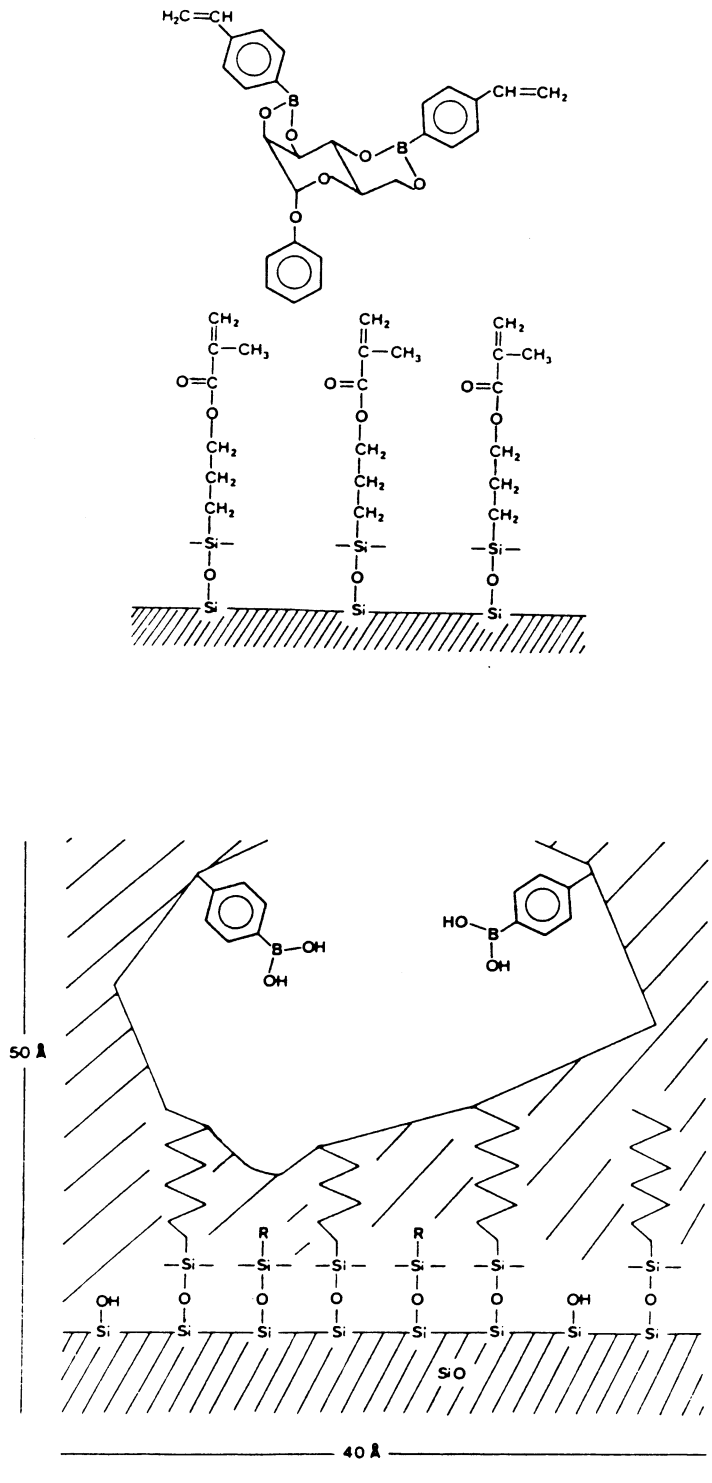
Schematic Diagram of Macroporous Polymer[14]
Figure 9

Imprinting on the Surface of Silica

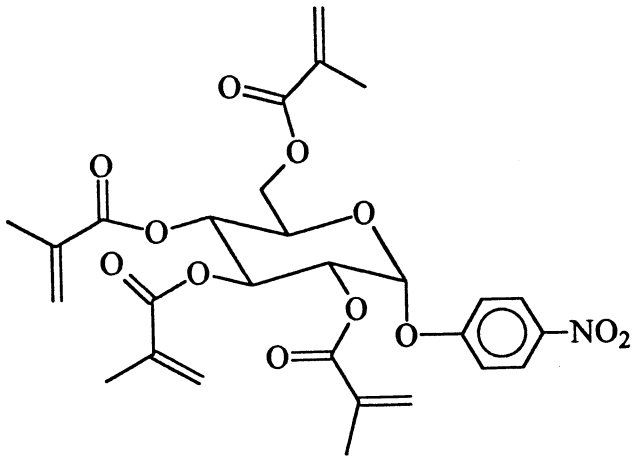
An interesting alternative to macroporous polymers is coating the silica surface[17] with an imprinted layer about 50Å thick. Instead of creating three-dimensional imprintings within a mass of polymer, three-dimensional molecular impressions in a thin polymer layer on the silica surface would be created. Its advantage, compared with the macroporous polymer, is that it is relatively easy to prepare. Since the silica already has high surface area around 300 m^2/g, learning how to prepare the high surface area macroporous polymer is not required. The ideal cavity should be situated close to the surface of the 50Å polymer layer for

greatest accessibility. A thickness of about 50 Å is a desired because it should both be thick enough to maintain the integrity of the cavity and be thin enough to assure that most cavities would occur close to the surface of the polymer. A diagram of the polymer formed on the surface of silica is shown in Figure 10. In the construction of a polymer layer, we used 4-nitrophenyl 2,3,4,6-tetra-O-methacroyl-α-D-glucopyranoside (**8**) as a monomer (monomer III), whose structure is shown in Figure 11 and whose detailed synthesis was reported by Jiang.[18] Styrene (**9**) and divinylbenzene (DVB) (**10**) were used as copolymer and crosslinking agents.

In the approach used by Wülff,[14] only two polymerizable groups were used since his results suggest that the number of binding/polymer formation groups on the template should be small. But examination of the relatively low α values for the resolution of racemic mannose by the polymer imprinted with his monomer having just two polymerizable units would suggest that a monomer with a larger number of polymerizable units to capture a greater amount of the stereochemical information of the glucose template might give better results. Glucose binding protein for example, is known to involve thirteen hydrogen bonds holding the glucose molecule in place.[19] In this research, since monomer III (**8**) has four binding sites, a cavity formed with this monomer should have greater depth and better selectivity. Since complete substitution on a sugar is the easiest reaction to complete, a tetra-substituted monomer would be a good choice for that reason as well.



Schematic Picture of Polymer Coated Silica Imprinted by Monomer I (6).[14]
Figure 10



8

The Structure of Monomer III (8).
Figure 11

The 4-nitrophenyl group should be a suitable aglycon with the infrared stretching frequencies of the nitro group providing a unique analytical marker. For the polymerizable units, a methacrylate ester is a good choice since it is easily copolymerized with styrene and DVB, as discussed later in the section on reactivity ratios.

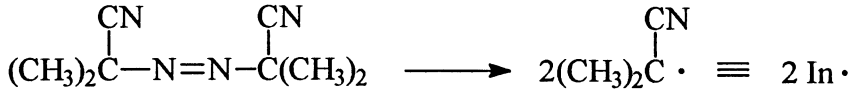
D. Polymers and Polymerization

Free radical polymerization mechanism

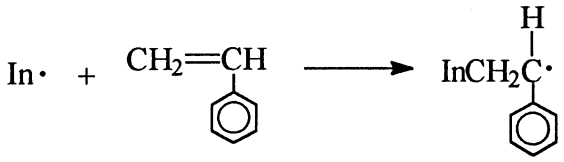
The polymerization of unsaturated monomers typically involves a chain reaction. Many organic reactions take place through intermediates having an odd number of electrons and, consequently, an unpaired electron. Such intermediates are known as free radicals. There is a wide variety of vinyl monomers that will undergo free radical polymerization including styrene, vinyl acetate, acrylate, and methacrylate monomers. The most common radical initiator is azobisisobutyronitrile (AIBN), which decomposes to generate a molecule of nitrogen plus two nitrile stabilized alkyl radicals. An outline of a free radical- initiated polymerization reaction mechanism is shown in Scheme 6.

The initiation step involves the decomposition of the initiator to yield two radicals where each radical is capable of initiating a polymer chain. The propagation or the growth step involves the rapid regioselective addition of additional monomer to the radical species. The propagation step is eventually terminated. Termination may occur by combination wherein two growing macroradicals interact to yield an inactive species. An alternate mode of termination is usually a disproportionation type reaction where two macromolecular radicals terminate each other. One abstracts a hydrogen atom from another to yield a saturated end group on one and a vinyl end group on the other.

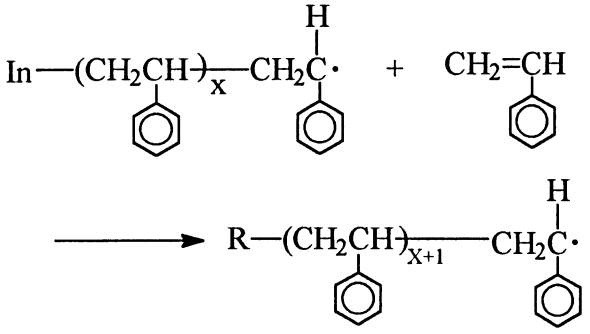
Initiation



AIBN

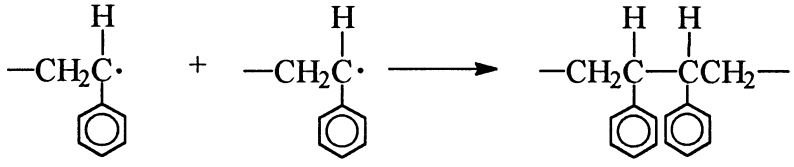


Propagation

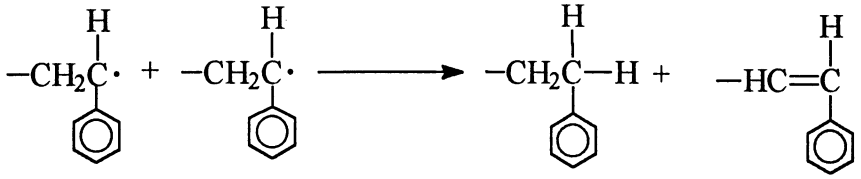


Termination

Combination:



Disproportionation:

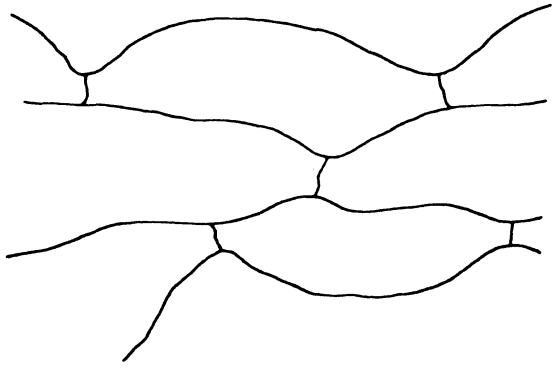


The Free Radical Reaction Mechanism of Polymerization
Scheme 6

There are essentially four important types of processes that should be mentioned in the radical polymerization reaction. First of all, one can have a bulk reaction where basically only the monomer and the initiator are used. Alternatively, a solution reaction process may be used which has monomer, initiator and a solvent present. Bulk and solution reactions are sometimes referred to as homogeneous processes. The other two processes of importance are often termed heterogeneous processes, and they are known as suspension and emulsion polymerization.

Crosslinked Polymers

A crosslinked or network polymer is one which has covalent linkages between the chains, as illustrated in Figure 12.[20]



Schematic Diagram of Crosslinked Polymer
Figure 12

The percentage of crosslinking is a ratio of moles of crosslinking agent to total moles of monomer material. For example, a polymer mixture of 99 moles of some vinyl monomer and 1 mole of crosslinking agent would be referred to as 1% crosslinking.

Copolymers

The term copolymer refers to a polymer having two or more different monomers incorporated into the same polymer chain. For example, if styrene and acrylonitrile are allowed to copolymerize in the same reaction vessel, a copolymer will be formed which contains both styrene and acrylonitrile residues.

It should be noted that the sequence of monomer units along a copolymer chain can vary according to the reactivity ratios and the mechanism and method of synthesis. Four different types of sequencing arrangements are commonly found.

Random copolymers. In random copolymers, no definite sequence of monomer units exists. A copolymer of monomers A and B might be depicted by the arrangement shown in Figure 13. Random copolymers are often formed when olefin monomers copolymerize by free radical processes.

Alternating copolymers. As the name implies, these copolymers contain a regular alternating sequence of two monomer units as shown in Figure 13. Olefin polymerization that takes place through ionic mechanisms can also yield copolymers of this type. The properties of the copolymer usually differ markedly from those of the two related homopolymers.

Block copolymers. Block copolymers contain a block of one monomer connected to a block of another, as illustrated in Figure 13. Block copolymers are usually formed by ionic polymerization processes. Unlike other copolymers, they retain many of the physical characteristics of the two homopolymers.

Graft copolymers. This copolymers occur when one monomer is grafted onto a backbone of the others to form branches as shown in Figure 13.

-A-B-B-B-A-A-B-B-A-A-A-B-B-B-A-A-A-B-B

Random Copolymer

-A-B-A-B-A-B-A-B-A-B-A-B-A-B-A-B-A-

Alternating Copolymer

-A-A-A-A-A-A-A-A-B-B-B-B-B-B-B-B-

Block Copolymer

```
B                 B          "graft"
B                 B
B                 B
AAAAAAAAAAAAAAAAA            "trunk"
    B
    B
    B
    B
```

Graft Copolymer

Several Types of Copolymers.
Figure 13

Reactivity Ratios

In 1936 Dostal[21] conducted the first study on the mechanism of copolymerization by assuming that the rate of addition of monomer to a growing free radical depends only on the nature of the end group on the radical chain. Thus monomers M_1 and M_2 lead to radicals of types $M_1\cdot$ and $M_2\cdot$ respectively. The simplest reaction sequence for random free radical chain copolymerization is given in Scheme 7.

Reaction	Rate
$M_1\cdot + M_1 \xrightarrow{k_{11}} M_1\text{-}M_1\cdot$	$k_{11}[M_1\cdot][M_1]$
$M_1\cdot + M_2 \xrightarrow{k_{12}} M_1\text{-}M_2\cdot$	$k_{12}[M_1\cdot][M_2]$
$M_2\cdot + M_1 \xrightarrow{k_{21}} M_2\text{-}M_1\cdot$	$k_{21}[M_2\cdot][M_1]$
$M_2\cdot + M_2 \xrightarrow{k_{22}} M_2\text{-}M_1\cdot$	$k_{22}[M_2\cdot][M_2]$

The Rate of Copolymerization Reaction[24]
Scheme 7

Here, one considers four possible reactions that as written may lead to either a copolymer unit being formed or a homopolymer unit being formed. In each case then, cross initiation of the other monomer by a different macroradical chain end will produce elements of a copolymer. Copolymers of this type are usually of interest because they can display a number of desirable averaged properties.

The reactivity ratio, r_1, for monomer M_1 is defined as $r_1 = k_{11}/k_{12}$, the ratio of rate constants k_{11} and k_{12}. It is the ratio of rate constants for a given radical adding to itself to that for its adding the other monomer. The reactivity ratio r_2 for monomer M_2 is similarly defined. There is a considerable amount of significance ascribed to the values of the reactivity ratios. As indicated in Table 1,[22] r values of between 0 and 1 will imply that two monomers will probably be able to be copolymerized in a fairly random fashion.

Table 1
Reactivity Ratios[22]

r values of $0 \rightarrow 1$	Imply monomers will copolymerize
$r_1 > 1$	Prefers to homopropagate
$r_1 \cong 0$	Prefers to alternate
$r_1 \cong r_2 \cong 1$	Prefers to alternate randomly

If either of the values is greater than one, that means that it would prefer to homopropagate rather than cross initiate the other monomer. On the other hand, as the reactivity ratio approaches 0, that implies that the growing chain end prefers to cross-initiate the other monomer rather than add to its own chain end. Perhaps the best situation might be when both reactivity ratios are approximately equal and their product is about 1. Such a system would produce a perfectly random copolymer.

In our research, the monomer and crosslinking agent are styrene (**9**) and

DVB (**10**) respectively. The monomer is 4-nitrophenyl 2,3,4,6-tetra-O-methacroyl-α-D-glucopyranoside (**8**), as shown in Figure 11, is also a crosslinking agent but represents only 3-5 mole percent of total polymer. The composition of the styrene-DVB mixture was adjusted so that 50% crosslinking was possible.

One point worth mentioning is why the vinyl groups of the carbohydrate monomer do not react with each other. From the structure, it is very clear that if the monomer vinyl groups reacted with each other, it would form eight or nine membered rings. These kinds of rings have the slowest formation rate[23] compared to the formation of ring of other sizes. Therefore, ring formation should not compete with radical copolymerization with the other monomer present.

However the ability of monomer III (**8**) to copolymerize with other monomers is of considerable importance. In this system, styrene (M_1) / methylmethacrylate (M_2), $r_1 = 0.52$ and $r_2 = 0.46$. This means that each radical adds the other monomer about twice as fast as its own[24] and the polymer formed will be fairly random in its composition. Some typical reactivity ratios are listed in Table 2.

There is some concern that the reactivity ratios for the methacrylate monomer III (**8**) and divinylbenzene/styrene might not be appropriate for extensive copolymerization and crosslinking. These concerns are relieved by comparison of several reactivity ratios in Table 2. The reactivity ratios of a number of alkyl methacrylates with styrene are similar. For example, the reactivity ratios of

cyclohexyl methacrylate (CMA) with styrene are $r_1 = 0.45$ and $r_2 = 0.52$. The methacrylate esters of glucose would presumably have similar ratios as other methacrylate esters, which are all of approximate the same value.[25]

Also, the commercially available DVB is only 55% pure, the rest being mostly meta and para isomers of ethylstyrene. Note that in Table 2 the reactivity ratios for the styrene, p-methylstyrene and m-methylstyrene with DVB are similar to that for styrene with DVB.

Table 2
Typical Monomer Reactivity Ratios

Monomer 1	Monomer 2	r_1	r_2
MMA	EGDM	1.49[26]	0.67
MMA	MAA	0.90[27]	0.60
MMA	2-vinyl pyrdine	0.30	1.10
MMA	styrene	0.52	0.46
CMA	styrene	0.45	0.52
EGDM	styrene	0.65	0.40
MMA	p-methylstyrene	0.41	0.44
MMA	m-methylstyrene	0.53	0.49

Note: MMA= methylmethacrylate; EGDM= ethylene glycol dimethacrylate
MAA= methacrylic Acid; CMA = cyclohexyl methacrylate

The polymer crosslinking is mainly determined by the mole percentage of DVB in the total polymer. Through different compositions of DVB, the polymer acquires different degrees of crosslinking. This is an important point because the selectivity of the imprinted polymers is crucially dependent on the polymer structure and that has a close relationship with its degree of crosslinking. Also the polymer should possess high rigidity to preserve the shape of the cavities after removing the template. This also can be done by high crosslinking. Wülff's results[14] show a dramatic increase in the separation factor α with an increase in the percent crosslinking. In addition to rigidity, the polymer must show some flexibility in the whole arrangement. The cavity must have some flexibility to allow a fast binding and exit of substances within the cavity. One indication of flexibility is the swellability of the polymer.

In Wülff's research,[14] ethylene glycol dimethacrylate (EGDM) was compared with p-DVB as a crosslinking agent. His results show that in polymers with 52% to 95% crosslinking, DVB gave low specificity due to its low swellability and the percentage of template molecule removed from cavity was also very low than EGDM. As a crosslinking agent, DVB produced highly rigid cavities with less flexibility. Presumably because of their rigidity, many cavities could not be freed of the template. The EGDM produced cavities which are flexible enough for fast binding and good template removal. A fairly large amount of pendant vinyl groups still remains in a styrene-DVB matrix.[28] While on the surface this would seem

unfortunate, a lower extent of crosslinking could provide extra flexibility for the polymer. Based on this, it could be that DVB with a 50% crosslinking could have similar flexibility as EGDM with 100% crosslinking.

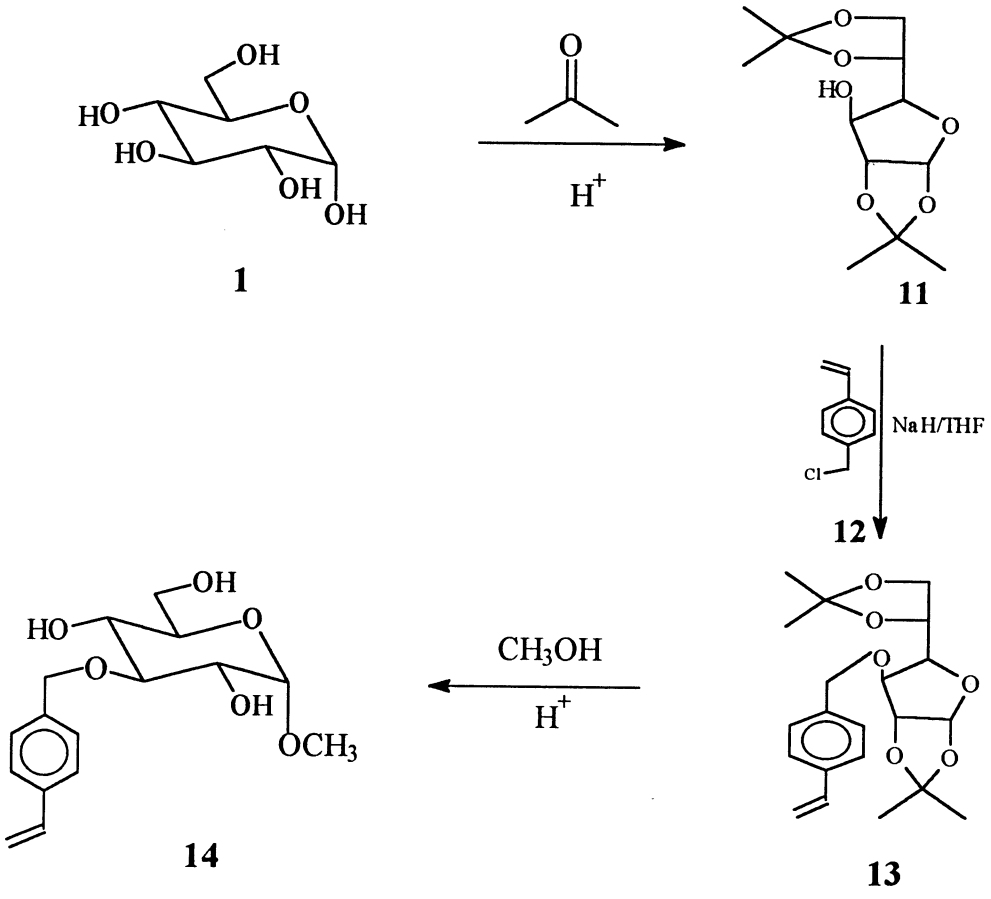
CHAPTER 2

Results and Discussion

Part A: The Syntheses of a New Monomer

The goal in this part of the research was to prepare a monomer based on glucose as a template and with functionality appropriate for executing a reaction within the cavity of the polymer. The strategy in this research was to use an α-glucopyranoside as a template molecule since sucrose has this feature. Based on this template, a monomer would be synthesized and then polymerized with a crosslinking agent to create a glucose-specific cavity in a three-dimensional, crosslinked polymer matrix such as polystyrene/DVB. The glucose monomer should retain the chair conformation that it has in sucrose.[29] This requires using blocking groups that will not distort the conformation of the pyranose ring. In addition, the aglycon should be at least as large as the fructose portion of sucrose so that upon polymerization, enough space in the matrix is provided for the fructose end. In the characterization of the polymer, it will be useful to have an analytical method available for the aglycon. A 4-nitrophenyl aglycon would seem appropriate.

As a demonstration of using the polymer cavity to carry out a regioselective reaction on the 3- position of the glucose as explained in Chapter 1, the monomer II methyl 3-O-vinylbenzyl-2,4,6-tri-O-methacroyl-α-D-glucopyranoside (**7**) was selected to fulfill this need. The proposed synthesis of monomer II (**7**) is outlined in Scheme 8.



1 11 12 13 14 7

Proposed Synthetic Route of Monomer II (7)

Scheme 8

In the proposed synthesis of monomer II (**7**), D-glucose (**1**) is allowed to react with two moles of acetone under acidic conditions to form the known 1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (**11**), commonly called diacetoneglucose. This is a common way to protect the glucose by ketal formation but, more importantly, leaves the 3-OH available for further reaction. Then **11** is treated with NaH followed by vinylbenzyl chloride (**12**) to form the 3-O-vinylbenzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (**13**). Methanolysis of the vinylbenzyl ether **13** should remove the two isopropylidene groups and concurrently regenerate the methyl glucopyranoside **14**. In the last step, **14** is treated with methacroylic anhydride in pyrdine to form monomer II (**7**).

The first intermediate **11** has been synthesized and characterized according to the literature.[30] The second intermediate **13**, was synthesized based on the procedure for the syntheses of 3-O-benzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (**15**).[31] The commercially available vinylbenzyl chloride starting material is a mixture of para and meta isomers, so the final product is also a mixture of isomers. Evidence for this mixture of isomers of **13** could be observed in the NMR spectrum. As a separate project, the pure vinylbenzyl chloride was prepared.[32] Based on this starting material, pure **13** was synthesized.

The third step was the methanolysis of the **13** under acidic conditions to form the next intermediate, methyl 3-O-vinylbenzyl-α-D-glucopyranoside (**14**). Based on NMR spectra evidence, the major product is the partially deprotected product, presumably the intermediate 3-O-vinylbenzyl-1,2-O-isopropylidene-α-D-glucofuranoside (**16**). This suggestion is based upon the fact that the parent diacetoneglucose loses the 5,6 ketal group first. Evidence for totally deprotected

product **14** was not observed in the NM spectrum. The same methanolysis reaction was attempted with the model compound **15** with similar results, partial deprotection. The product is presumably 3-O-benzyl-1,2-O-isopropylidene-α-D-glucofuranoside (**17**).

A ^{1}H NMR spectrum of diacetoneglucose (**11**) (Figures 14 and 15) was recorded using $CDCl_3$ as the solvent. The four methyl groups appear in the 1.33-1.50 ppm range as four singlets. The signal of four methyl groups is very easy to identify and was used as our basis for determining the next deprotection reaction. The partially deprotected product has two methyl groups remaining and its NMR spectrum shows two methyl signals around 1.4 ppm. The totally deprotected product should exhibit no methyl group signals. The anomeric proton appears at 5.95 ppm, the only proton bonded to a carbon bearing two oxygens. It is easily identified by its downfield chemical shift and multiplicity as a doublet with a coupling constant of 3.6Hz. The IR spectrum, Figure 16, exhibits a strong stretching frequency at 3450 cm^{-1} indicating the existence of the -OH group. Strong absorption by aliphatic C-H stretching appears just below 3000 cm^{-1} and in the 1000-1200 cm^{-1} region, the strong absorption is due to the isopropylidene groups.

A ^{1}H NMR spectrum of 3-O-(p-vinylbenzyl)-1,2:5,6-di-O-isopropylidene-α-D-glucopyranoside (**13**) was obtained in $CDCl_3$ and is shown in Figure 17. The benzene ring is a multiplet symmetrically centered at 7.36 ppm. The vinyl group is located at 6.67, 5.77 and 5.23 ppm. The signal for the benzyl protons should appear as singlet around 4.60 ppm, but it overlaps with the H-2 proton. The anomeric proton is at 5.88 ppm and the four methyl groups appear from 1.30 to 1.48 ppm. The NMR spectrum of the meta, para isomer mixture has also been

obtained in $CDCl_3$ and are shown as Figures 18 and 19. The difference is in the shape of the signal for the four protons in the benzene ring which is not symmetrical. The IR spectrum of **13** was obtained as shown in Figure 20.

A ^1H NMR spectrum of 3-O-benzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside, (**15**), was also obtained in DMSO-d_6, Figure 21, and its IR spectrum is shown in Figure 22.

A ^1H NMR spectrum of the 3-O-benzyl-1,2-O-isopropylidene-α-D-glucofuranoside (**17**) was obtained in DMSO-d_6 and is shown as figure 23. The two singlets due to the remaining isopropylidene group appear at 1.45 ppm.

From previous kinetic studies by other researchers,[33] it is known that there is a competition between partial deprotection and total deprotection. The rate constants for the deprotection of the 5,6-O-ketal (k_1) and 1,2-O-ketal (k_2) in 1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (**11**) are similar but when there is a 3-O substituent, the 5,6 blocking group tends to be deprotected more easily than that at the 1,2 position. Also an increase in acidity has a greater effect on the 5,6-O-ketal site than on that of the 1,2-O-ketal and the rate constant ratio, k_1/k_2, decreases as the chain length of the 3-O-substituent increases. This is due to the steric hindrance of the 3-O group which has more influence on the 5,6-O-ketal.

There are some reaction media that do deprotect both acetals of some derivatives, for example, water-acetic acid[34] or methanol-HCl.[35] The acid-solution system used in the reaction reported here was ion exchange resin Dowex-50 H^+ in anhydrous methanol, refluxing for 24 hours or longer. The reason for using methanolic conditions is that the product should be the stable methyl α-D-glucopyranoside instead of the mixture of the reactive glucopyranose anomers and

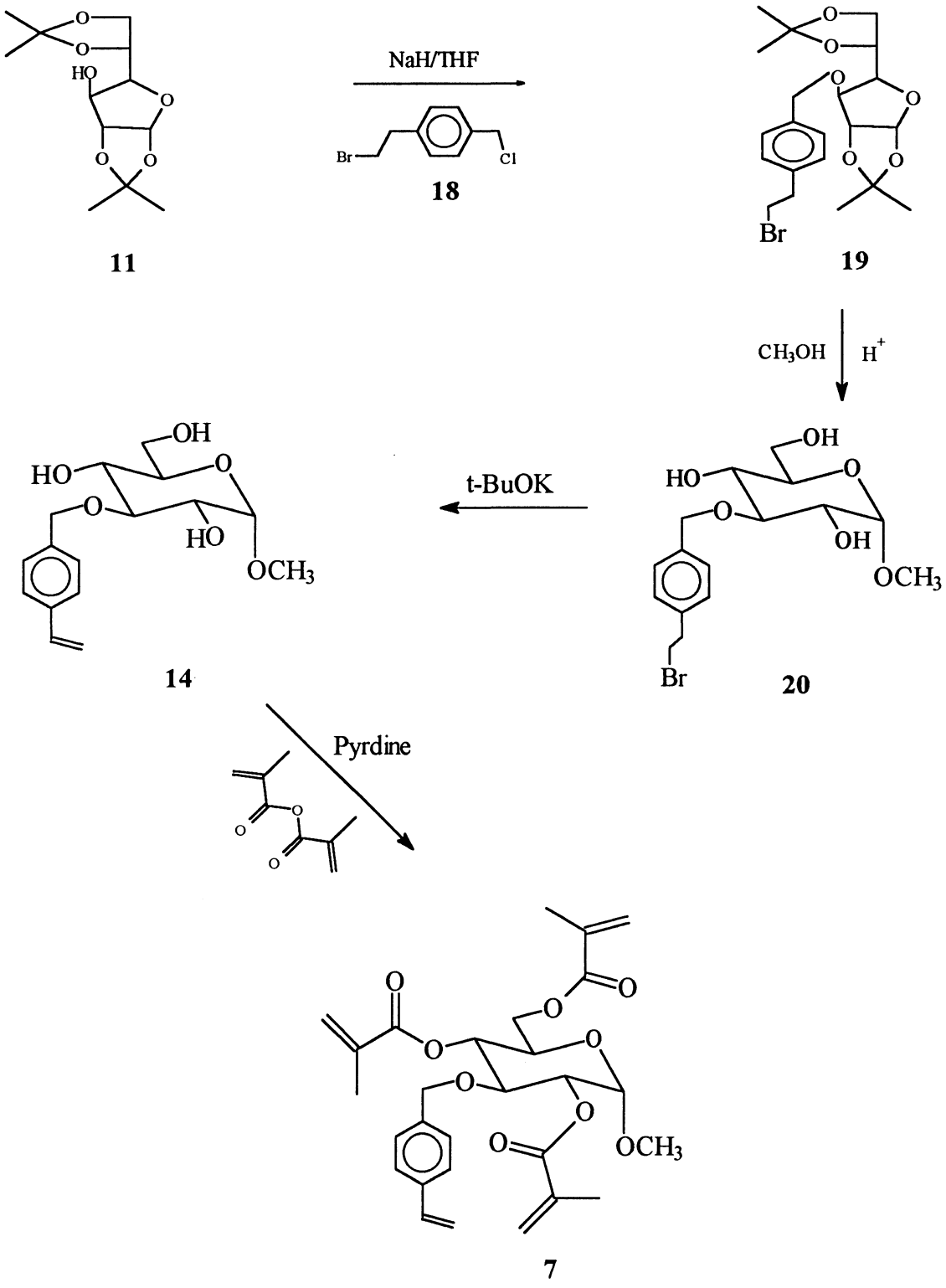
this saves a step in the proposed synthesis. The reaction was monitored by TLC with a hexane-acetone (1:1) eluent. After 4 hours, the main spot in the TLC plate was a spot at $R_f = 0.5$ while the starting material exhibits $R_f = 0.75$. But no new spots appeared even after the reaction continued 24 hours or longer. The desired product should have $R_f < 0.5$. All the conditions attempted failed to produce the fully deprotected product. The proton NMR spectrum should show the disappearance of all four methyl groups, but two methyl groups, assumed to be 1,2-isopropylidiene derivative **16**, remained. Several other sets of conditions have been used and the results are shown in Table 3.

Table 3
Results of Several Deprotection Reaction Attempts

Substrate	Acid	Medium	Time	Deprotection
15	H_2SO_4 (*dil*)	CH_3OH Reflux	2-10 hrs	Partial
15	Acetic acid(50%)	H_2O 45°C	2-10 hrs	Partial
15	Dowex-40W(H^+)	H_2O-CH_3OH Reflux	2-24 hrs	Partial
13	HCl(5%)	CH_3OH Reflux	2-36 hrs	Partial
13	H_2SO_4 (*dil*)	CH_3OH Reflux	4-24 hrs	Partial
13	Dowex-40W(H^+)	CH_3OH Reflux	4-48 hrs	Partial
13	Tosylate	Ethanol Reflux	2-48 hrs	Partial

Mehltretter[36] prepared 3-O-stearoyl-D-glucose in 52% yield using 12N HCl in ether-water (1:1) solution. Glacet[37] obtained 3-O-palmitoyl-D-glucose in 78% yield by the same method, and Gouéth[33] used a 12N HCl in dioxane solution (4:1) and obtained total deacetaliztion in good yield. So based on these results, a more concentrated acid should be used to get the completely deprotected product.

Another problem in the synthetic route is that the vinyl group is very easily polymerized. For the syntheses of **13**, the commercial vinylbenzyl chloride has an inhibitor in it and during the reaction it was not removed but still, partial polymerization was observed. When doing the methanolysis reaction to produce **14**, it is very easy to get the polymerized product. To avoid premature vinyl group polymerization, an alternative route was attempted as outlined in Scheme 9. Using 4-(2-bromoethyl)benzyl chloride (**18**) instead of vinylbenzyl chloride (**12**) would allow protection of the double bond and prevent premature polymerization. The formation of the resulting bromoethylbenzyl ether **19** would be followed by the removal of the two acetal groups forming **20**. This would have been followed by strong basic conditions where dehydrohalogenation should form the vinylbenzyl group forming **14**. But the results were not satisfactory, since the first step for formation the bromomethyl ether was also in strongly basic conditions allowing a side reaction, dehydrohalogenation, to occur, thus the vinylbenzyl ether was prematurely the final product.



Alternative Route for the Synthesis of Monomer II (7)

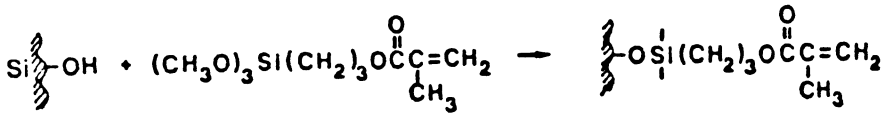
Scheme 9

Part B: Polymerization Reactions on Silica

Analogous to Wülff's former work,[38] the goal in this part of the research was to prepare polymer layers imprinted with the template monomer on silica using 4-nitrophenyl 2,3,4,6-tetra-O-methacroyl-α-D-glucopyranoside, (**8**). Silica with 150 Å mean pore diameter was chosen. The silica used here was Davison Chemical silica gel 25-35 μm with surface area around 300 m^2/g. The polymer layer should have a thickness of at least 40Å in order to cover the template molecule completely. Small pores of 60 and 100Å would be completely filled up, whereas larger pores would be coated on their inner surface but still allow free diffusion through them.

Polymer layers can be fixed on the silica surface by physical adsorption or by chemical bonds.[39] Especially advantageous is covalent bonding of a monomeric silane that carries unsaturated bonds, *e.g.*, vinyl groups, and then this could be followed by copolymerization with added monomers on the surface.[40]

According to the procedure published by Mosbach,[41] the commercially available 3-methacryloxypropyltrimethoxysilane (**21**) was dissolved in toluene and was allowed to bond to the surface of silica via siloxane bonds, as shown in Scheme 10.



Silica **21** Methacrylate-silica

Preparation of Methacrylate Silica[41]
Scheme 10

The amount of the methacrylate **21** used was calculated based on assumption that the material would occupy about 8 μmole/m^2 on the surface. To determine the actual coverage, Mosbach[41] used a bromine water titration as quoted: "The concentration of immobilized methacrylate groups was determined according to the following methods. Dried methacrylate-silica (*ca.* 70mg) was suspended in 10mL of water. Diluted bromic water was added to the suspension until a faint color remained. The hydrobromic acid generated was titrated with 0.5*M* sodium hydroxide to pH 5.0. Two controls, unsubstituted silica treated in the same way, and methacrylate silica with no bromic water added, gave no consumption of sodium hydroxide. The concentration of double bonds on the methacrylate-silica was 22 μmol/g." Repeating this procedure would be very difficult on such small percentage of methacrylate coverage, because in using 0.5*M* sodium hydroxide to titrate the HBr that was generated by addition to the double bond, only 0.00308mL of 0.5M sodium hydroxide would have been consumed! This suggests that some sort of error was introduced during the writing of that paper. Another way to calculate the surface coverage is by elemental analysis. The surface coverage is calculated from carbon percentages derived from elemental analysis of the chemically bonded phase. Hemetsberger[42] and Berendsen[43] have calculated the immobile phase coverage with Equation **1**.

chemically bonded phase. Hemetsberger[42] and Berendsen[43] have calculated the immobile phase coverage with Equation **1**.

$$\text{N coverage } (\mu\text{mol/m}^2) = \frac{10^6 \cdot P_c}{1200\, n_c - P_c \cdot (M-1)} \cdot \frac{1}{S} \qquad \mathbf{1}$$

P_c is the measured carbon percentage.
n_c is the number of carbon atoms in the bonded silane molecule.
M is the relative molecular weight of silane molecule.
S is the surface area of the silica in m^2/g.

Elemental analysis of this treated silica gave 6.57%C, 1.14%H. Using Equation **1** the coverage was calculated to be 2.49 $\mu mol/m^2$. Compared with Wülff's result,[17] the number here is reasonable. The results are shown in Table 4 along with the BET surface area determination. As expected, the silica after treatment was found to have a reduced surface area.

Table 4
Properties of Silica and Modified Silica

Mean pore Diameter (Å)	Surface area of silica (m^2/g)		Con. of Methacrylate residue on modified silica ($\mu mol/m^2$)
	Before Treatment	After Treatment	
150	288	219	2.49

Bulk polymers are usually prepared in the presence of inert solvents to produce macroporous polymers. In the case of a thin layer of polymer on silica, macroporosity is not important. The solvent, however, was necessary to dissolve both the monomers and the initiator, and to obtain a uniform layer by evaporating the excess of solvent. The template monomer amount is about 5 mole percent of the monomer materials. This means that every monomer should be surrounded by about nineteen other monomer units, in this case, the styrene and DVB. This would ensure that the template would have enough material around it to support the cavity. Otherwise, after removing the template, the cavity could collapse. As for the polymerization materials, styrene-DVB as a copolymer with 50% crosslinking were used. The commercial crosslinking agent DVB is available only as mixture of 55% of meta and para isomers of DVB and 45% of meta and para isomers of ethylstyrene. So for a 50% crosslinked polymer, enough styrene was added to the commercial DVB to make the "styrene like" molecules 50% of the mixture. The amount of the total polymerization material used was calculated based on forming a 50 Å thick layer over 219 m^2/g of treated silica surface. Polymerization was performed at 70 ^0C in the dry state using AIBN as an initiator. Extraction experiments showed that most of the monomer was polymerized within the layer. The BET surface area of the silica polymer was 247 m^2/g. For comparison , the IR spectra of untreated silica and treated silica are shown in Figures 24 -25.

The concentration of template in the hydrolysis solution could be estimated

quantitatively by evaporation and weighing, by direct measurement of the optical rotation, or, as done here, by spectroscopy based on the absorption by the 4-nitrophenyl chromophore, log ε = 4.07 at 317 nm. The UV spectrum of the hydrolysis solution is shown in Figure 26, and exhibits an absorption peak at λ_{max} = 298 nm, similar to the UV spectrum of the template molecule λ_{max}= 296 nm is shown in Figure 27. The potassium salt of 4-nitrophenol exhibits a λ_{max} at 398 nm, compared to 317 nm for the 4-nitrophenol. This is due to the proton on the hydroxyl group is being removed, so the resonance is extended shifting λ_{max} from 317 to 398 nm. The UV spectrum of 4-nitrophenol is shown in Figure 28. With the template molecule, there is no such shift in λ_{max} in basic solution. So from the preliminary analysis, it seems that there is something being removed by hydrolysis from the cavity. Whether or not it is the template molecule or just glycosidic cleavage to produce the aglycon is still under investigation. Further research will concentrate on the HPLC analysis of the hydrolysis materials.

CHAPTER 3

CONCLUSION

The partial syntheses of a new monomer, methyl 3-O-vinylbenzyl-2,4,6-tri-methacroyl-glucopyranoside (**7**) has been completed. The complete deprotection and the easily polymerizable vinyl group are sources of difficulty. Further studies could consider introducing a vinyl protecting group. As for the methanolysis of the protected vinylbenzyl ether, ^{1}H NMR evidence shows that one of the isopropylidene groups, probably that at the 1,2-position, has not been removed. Further research should consider stronger conditions such as more concentrated acid but at the risk of polymerization.

UV spectroscopic analysis of the hydrolysis solution from the polymer suggests the existence of 4-nitrophenol. This indicates that the glycosidic linkage between the glucose portion and the aglycon may be decomposed. Beer's law plots of the template molecule and 4-nitrophenol have been done and the quantitative analysis is still under study.

The surface of silica can be coated in a simple way by thin layers of polymer which presumably contain cavities obtained by imprinting with the template. Compared with a macroporous polymer, this is an easy way to prepare non-swellable particles of a desired particle size. Further research should be explored in using new monomers with different binding sites and high percentage crosslinking polymer by using new crosslinking agents.

CHAPTER 4

EXPERIMENTAL SECTION

General Methods: All reactions were run in pre-oven dried (120 ^{0}C) glassware and performed under a nitrogen atmosphere unless otherwise stated. Proton (^{1}H) and carbon (^{13}C) NMR spectra were obtained on a General Electric QE-300 (300 MHz) Fourier Transform NMR Spectrometer and chemical shifts are reported in parts per million (ppm) relative to 1% tetramethylsilane (TMS). Peak multiplicities are abbreviated as follows: singlet, s; doublet, d; doublet of doublets, dd; triplet, t; quartet, q; multiplet, m. Infrared spectra were recorded on a Nicolet model DXB-20 Fourier Transform Infrared Spectrophotometer and a Perkin-Elmer 1310 Infrared Spectrophotometer; absorption values are reported in wavenumbers (cm^{-1}). Infrared spectra of the modified silica were recorded with Nicolet model DXB-20 FTIR. Since the spectra of the silica polymer from KBr pellets were too weak, it was obtained from the pure material. The UV spectra were recorded with Sahmaizu 1300 UV-Visible Spectrophotometer. Thin-layer chromatography (TLC) was performed on Analtech silica gel GF chromatography plates. Plates were visualized with an ultraviolet source. All reagents were pre-distilled for maximum dryness and purity before the start of each reaction. All melting points were obtained on a Fisher-Johns cover glass melting point apparatus and are uncorrected. The sample for elemental analysis for carbon and hydrogen was dried at 100 ^{0}C and ~1.5 Torr during 12 hours. The elemental analysis was performed by Galbraith Laboratories,

Inc. (Knoxville,TN). The usual column and flash chromatography were carried out with Fisher 60-200 Mesh Silica Gel S-704. Single point determination of BET surface area was carried out with a Quantasorb analyzer using 0.30 mole% of N_2 in He. For the determination of the surface area, the samples were dried for 24 hrs under vacuum at 100 ^{0}C in an Abderhalden apparatus and degassed under N_2 at 150 ^{0}C for two hours. THF was dried using potassium with benzophenone as an anhydrous indicator and then freshly distilled prior to use. Pyridine was dried by refluxing with potassium hydroxide and distilled prior to use. All reactions requiring anhydrous conditions were performed under a positive pressure of nitrogen. All the chemical reagents were purchased from Aldrich unless mentioned additionally.

4-Nitrophenyl 2,3,4,6-Tetra-O-Methacroyl-α-D-Glucopyranoside (8).[18] In a 150 mL E-flask, 4-nitrophenyl α-D-glucopyranoside (0.58 g, 1.94 mmols) was dissolved in 50 mL of previously dried pyridine. Methacrylic anhydride (2.9 mL, 19.4 mmols) was added to this mixture. Stirring was continued at room temperature for seven days. The mixture was then poured with stirring into a beaker containing a mixture of ice and water. Then 15 mL of ether was added with stirring and the aqueous layer was twice extracted with 10 mL of ether. The ether layers were combined, washed once with water then with saturated sodium bicarbonate solution until basic, then add sulfuric acid until neutral and again washed with water. The ether solution was dried over magnesium sulphate for 24 hours. The solvent was removed under reduced pressure on a rotary evaporator. Pure white crystals were recovered from 95% ethanol to give 0.67 g (1.17 mmols, 61%); m.p. 174-175 ^{0}C; Lit, 173-174.[18] ^{1}H NMR and FTIR spectra are in agreement with those reported.[18]

1,2:5,6-di-O-isopropylidene-α-D-glucopyranoside (11).[30] Anhydrous D-glucose (10.0 g, 0.09 mols), in a 300 mL three neck flask, was stirred vigorously with 200 mL of acetone in an ice bath. Sulfuric acid (96%, 10 mL) was added in 2 mL portions at 10-15 min. intervals, while maintaining the temperature at 5 to 10 ^{0}C. After the addition of sulfuric acid, the vigorous stirring was continued 5 hr, allowing the temperature to rise gradually to 20-25 ^{0}C. The solution was cooled again with an ice bath, and 50% sodium hydroxide solution was added, with

stirring, to near neutrality. The addition was done slowly to avoid heating. A small amount of solid sodium hydrogen carbonate was added to maintain the solution near neutrality. After standing overnight, the salts were removed by filtration, and the acetone solution was concentrated under reduced pressure to a thick syrup which solidified upon standing. The mixture was dissolved in chloroform on a water bath, and the solution was extracted with water. The chloroform solution was then washed with water, and the water solution was washed with chloroform, The respective water and chloroform solutions were combined. The chloroform solution containing the product, diacetoneglucose, was concentrated under reduced pressure to a syrup and finally recrystallized from cyclohexane to give 6.3 g (41%). M.p. 110 ^{0}C; reported[27] 109-113 ^{0}C. ^{1}H NMR ($CDCl_3$) δ: 5.95 (1H d, H-1), 4.52 (1H dd, H-2), 4.05-4.35 (4H m, H-4,-5,-6,-6'), 3.97 (1H dd, H-3), 1.50 (3H, s), 1.43 (3H, s), 1.37 (3H, s), 1.33 (3H, s). IR (KBr): 3450, 2986, 2874, 2657, 1455, 1370, 1227, 1049, 939, 856, 785, 694, 528cm^{-1}.

3-O-Vinylbenzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside(13).[31] In a 50 mL round bottom flask, diacetoneglucose (**11**) (2.60 g, 10.0 mmols), was dissolved in 25 mL of anhydrous THF. In a nitrogen filled glove bag, NaH, 65% dispension in oil, (0.050 g, 20 mmols) was carefully added to THF solution while stirring vigorously until H_2 evolution ceased. Then, $IN(Bu)_4$ (0.01 g) and the m,p-vinylbenzyl chloride (**12**) (2.0 mL, 10 mmols) were added to the solution. The

reaction was stirred for 24 hr at room temperature and monitored by TLC, petroleum ether - ethyl acetate (10:1) until the size of the spot (R_f = 0.4) of the starting material no longer decreased. The solvent was removed at reduced pressure and the residue dissolved with 35 mL of petroleum ether (b.p.60-80 °C). The petroleum ether solution was washed with water, dried with anhydrous calcium chloride, filtered and concentrated under reduced pressure to a syrup. The crude product, a mixture of vinylbenzyl chloride and product, was purified by column chromatography[44] on silica gel with petroleum ether:ethyl acetate (10:1) to give 1.1g (36%) of product as a yellow oil. ^{1}H NMR ($CDCl_3$) δ: 7.36 (4H, m, H-9,-10,-12,-13), 6.67 (1H, dd, H-14), 5.88 (1H, d, H-1), 5.77 (1H, d, H-15), 5.23 (1H, d, H-16), 4.60 (2H, m, H-7,-7'), 4.33 (1H, m, H-2), 4.01-4.15 (4H, m, H-4,-5,-6,-6'), 3.98 (1H d, H-3), 1.48 (3H, s), 1.42 (3H,s), 1.37 (3H, s), 1.30 (3H, s). IR (neat): 3446, 2988, 2933, 2899, 1627, 1375, 1238, 1163, 1074, 1019, 841.8 cm^{-1}.

3-O-Benzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (15).[31] In a 50 mL round bottom flask, diacetoneglucose (**11**) (0.260 g, 1.0 mmole) was dissolved in 25 mL of anhydrous THF. In a nitrogen filled glove bag NaH (0.050 g, 2.0 mmols) was carefully added to THF solution and stirred vigorously until H_2 evolution ceased. Then, $IN(Bu)_4$ (0.01 g) and benzyl bromide (0.25 mL 1.0 mmole) were added to the solution. The reaction was stirred for 24 hr at room temperature and monitored by TLC petroleum ether - ethyl acetate (10:1) until the size of the spot

of the starting material no longer decreased. The solvent was removed at reduced pressure and the residue dissolved with 35 mL of petroleum ether (b.p. 60-80 °C).The petroleum ether solution was washed with water, dried with anhydrous calcium chloride, filtered and concentrated under reduced pressure to a syrup. The crude product, a mixture of benzyl bromide and product was purified by column chromatography[44] on silica gel with petroleum ether:ethyl acetate (10:1) to give 0.16 g (40%) of product as a yellow oil. ^{1}H NMR (DMSO-D_6) δ: 7.36 (5H, m, H-9,-10,-11,-12,-13), 5.85 (1H d, H-1), 4.70 (2H, H-7,-7'), 4.52 (1H d, H-2), 3.90-4.30 (4H m, H-4,-5,-6,-6'), 3.78 (1H, dd, H-3), 1.50 (3H, s), 1.43 (3H, s), 1.37 (3H, s), 1.33 (3H, s). IR (neat): 2980, 2920, 2880, 173, 1450, 1250, 1010, 856, 748, 697 cm^{-1}.

Methanolysis of 3-O-Vinylbenzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (16). A solution of **13**, (0.10 g, 0.27 mmole) was dissolved in methanol (15 mL). The H^+ form of the ion exchange resin Dowex-50W-4X, (0.6 g) was added and this mixture was stirred for 24 hr at room temperature. TLC (eluent hexane-acetone (1:1)) indicated that the starting material had reacted almost completely to give a compound (R_f = 0.38) and a second product presumed to be methyl 3-O-vinylbenzyl-α-D-glucoside (R_f = 0.05). The solvent was removed by reduced pressure and the crude product was purified by column chromatography with hexane-acetone.

Methanolysis of 3-O-Benzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (17). A solution of **15** (0.10 g, 0.26 mmole) was dissolved in methanol (15 mL) with ion exchange resin, Dowex-50W-4X (0.6 g) and this mixture was stirred for 24 hr at room temperature. TLC (eluent hexane-acetone (1:1)) indicated that the starting material had reacted almost completely to give a new compound (R_f = 0.38). The solvent was removed by reduced pressure and the crude product was purified by column chromatography with hexane-acetone (1:1). ^{1}H NMR (DMSO-d_6) δ: 7.38, 5.95, 4.70, 4.60, 3.40-4.25, 3.35, 1.40, 1.50.

Preparation of Modified Silica.[41] Davison Chemical Silica Gel 25-35 μm (20.0 g) was dried (surface area 288 m^2/g) in a three-necked flask under vacuum (150-200 °C) for 4 hr. Potassium-dried toluene (250 mL) was then added via a separation funnel, still under reduced pressure, followed by 3-methacryloxypropyltrimethoxysilane (**21**) (5 mL, 16 mmols) and triethylamine (300 uL). The stirring mixture was continuously refluxed under nitrogen. The methacrylate silica was washed with 500 mL of toluene followed by 500 mL of acetone and 200mL of diethyl ether and finally dried under vacuum for 12 hr at 100 ^{0}C, giving 21.8 g of product. BET surface area: 219 m^2/g. Elemental analysis: C 6.57%, H 1.14%. The surface coverage was determined by elemental analysis to be 2.49 μmole/m^2.

Preparation of Silica Polymer.[17] Modified silica (5.0 g) was suspended in chloroform. 4-Nitrophenyl 2,3,4,6-tetra-O-methacroyl-α-D-glucopyranoside (**8**) (1.34 g, 2.35 mmole, 5 mole% of total polymer) was added. A 5.70 mL aliquot of a solution composed of 1.20 mL of stryene and 4.50 mL of commercial 55% DVB was added, along with AIBN (10 mg), to the chloroform solution. After stirring for 15 min and sonication for 20 min in ultrasonic bath to achieve uniform coverage of the substances on the silica, the excess solvent was removed by reduced pressure, without heating to avoid prepolymerization, until the silica appeared dry and the particles no longer adhered to each other. Before polymerization, the flask was carefully degassed three times by evacuating and filling the flask with nitrogen. The flask, under a slight pressure, was heated at 70 ^{0}C for three days. Afterwards, the silica was washed with acetone, water and methanol to remove all the unreacted material. The wash was examined for traces of the monomer by being made acidic and washed with ether to remove any styrene and DVB from the mixture. ^{1}H-NMR spectrum of the ether extract revealed no traces of the monomer suggesting that all the monomer had been consumed during the reaction. BET surface area measurement: 247 m^{2}/g.

Hydrolysis of The Silica Polymer.[17] A 0.055M solution of KOH in water was prepared by dissolving 3.10 g KOH in water and diluting to 1.0 L. To a 250 mL round bottom flask with 100 mL KOH solution was added 2.00 g of the silica polymer while stirring with a magnetic stirrer. The suspension was stirred in room temperature for 24 hr. After hydrolysis, the polymer was filtered and washed with 2x20 mL of acetone, 2x30 mL of water and 20 mL of acetone to remove any unreacted material. The polymer was transferred to a Soxhlet extractor for further extraction overnight with acetone and then dried to constant weight. The UV spectrum of the polymer hydrolysis in methanol showed a strong absorption at 298 nm.

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SPECTRA

Figure 14: ^{1}H NMR Spectrum of 1,2:5,6-Di-O-isopropylidene-α-D-glucofuranoside (11)

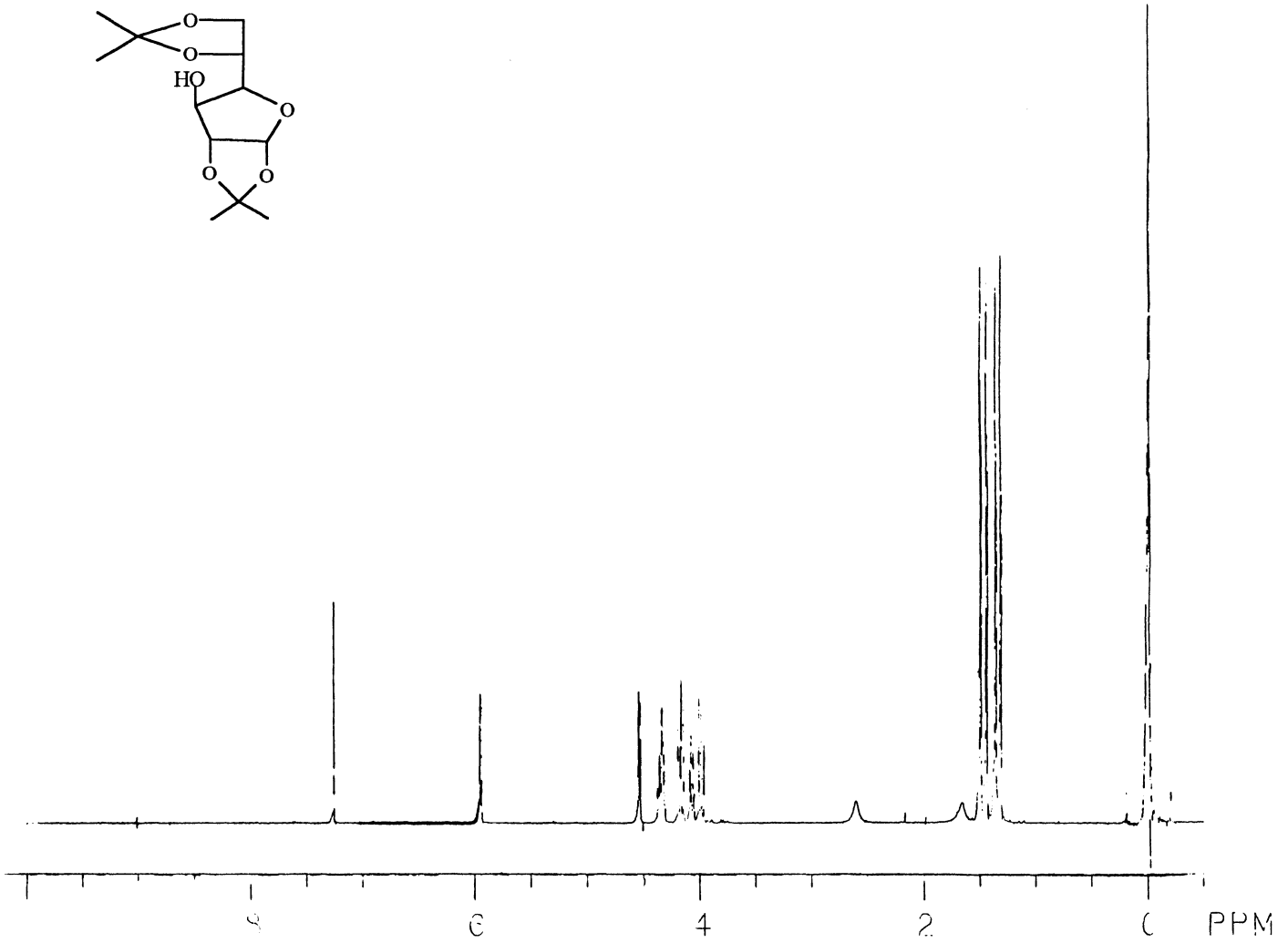

Figure 15: Expanded ^{1}H NMR Spectrum of 1,2:5,6-Di-O-isopropylidene-α-D-glucofuranoside (11)

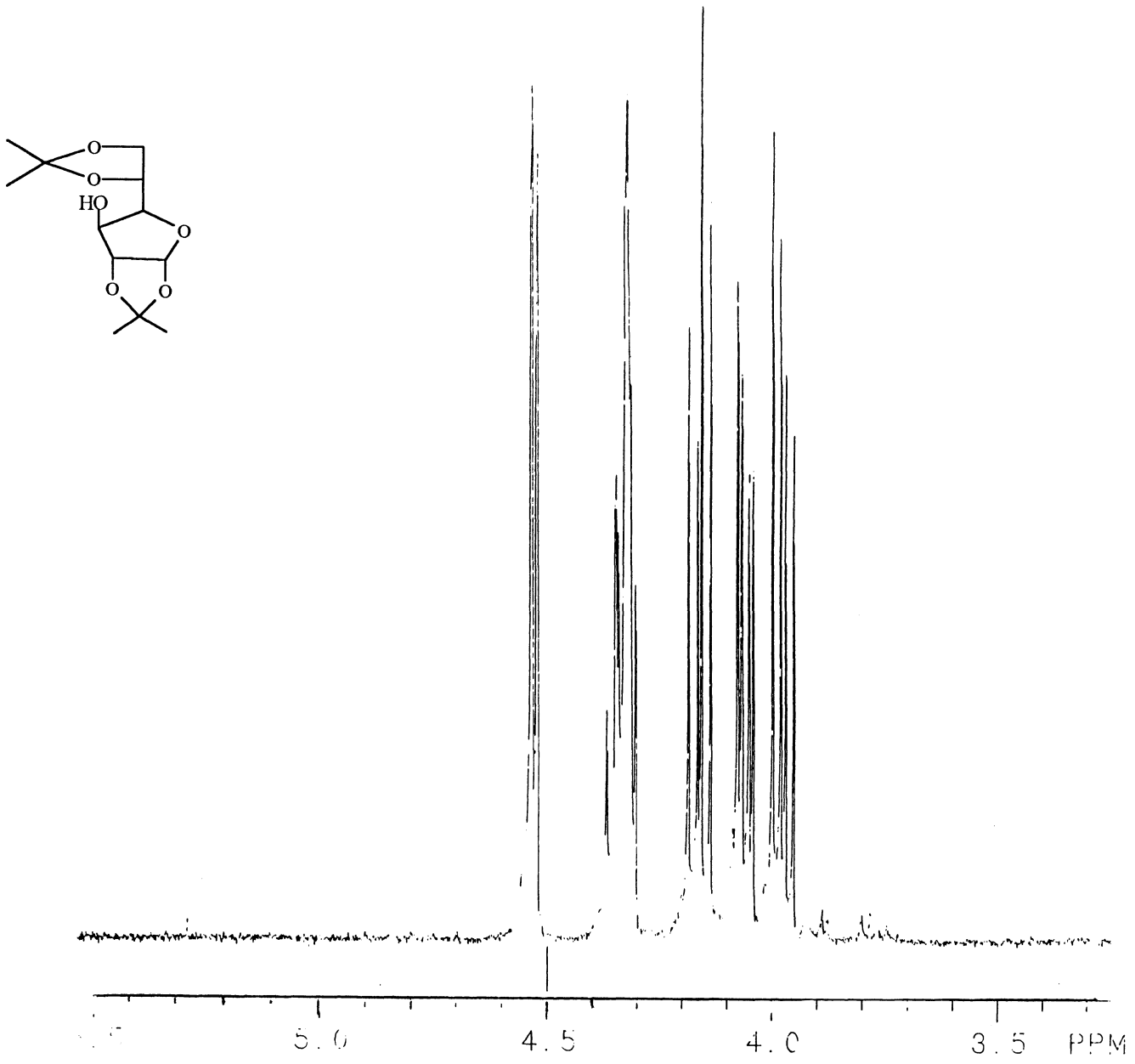

Figure 16: IR Spectrum of 1,2:5,6-Di-O-isopropylidene-α-D-glucofuranoside (11)

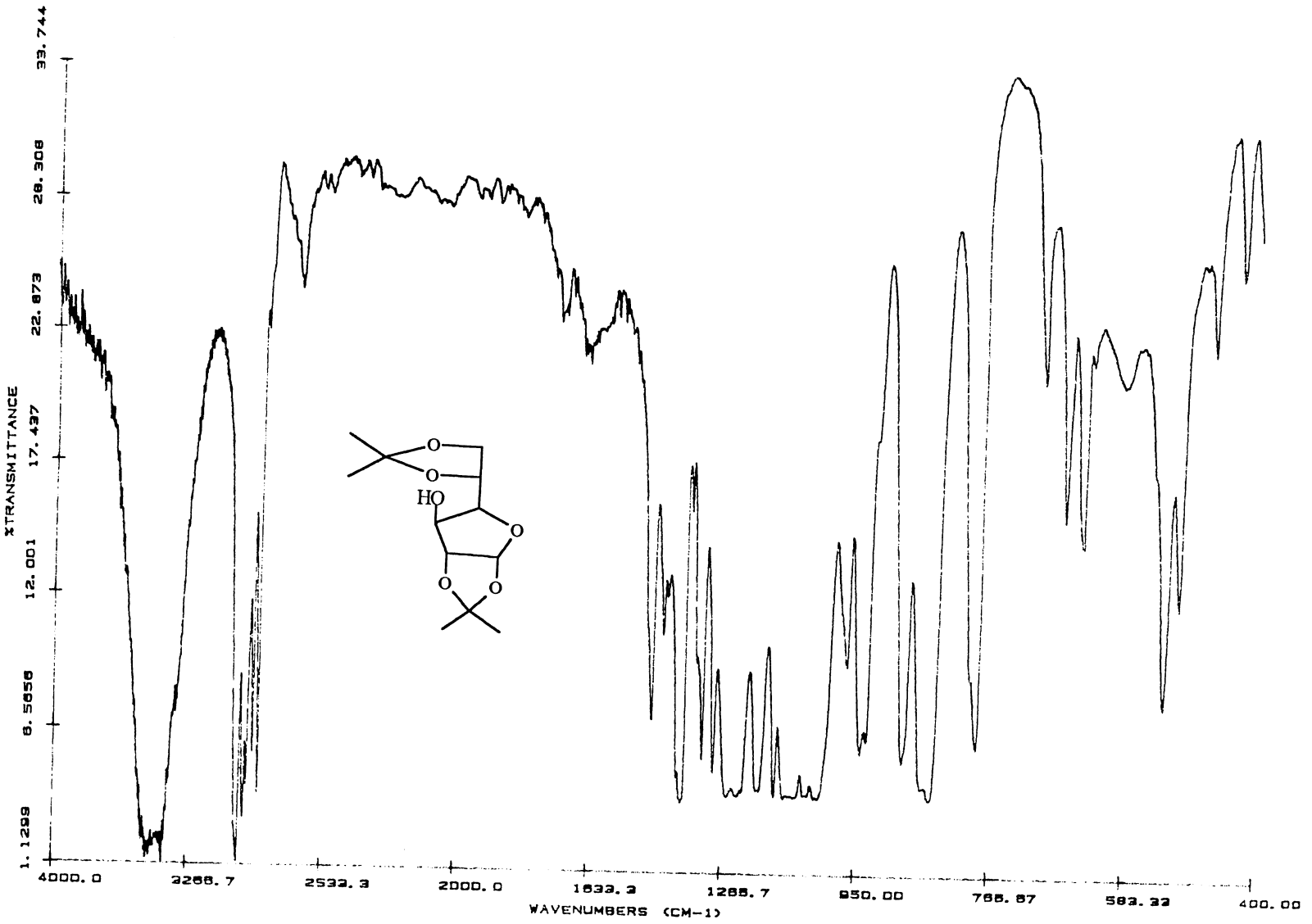

Figure 17: ^{1}H NMR Spectrum of 3-O-(p-Vinylbenzyl)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (13)

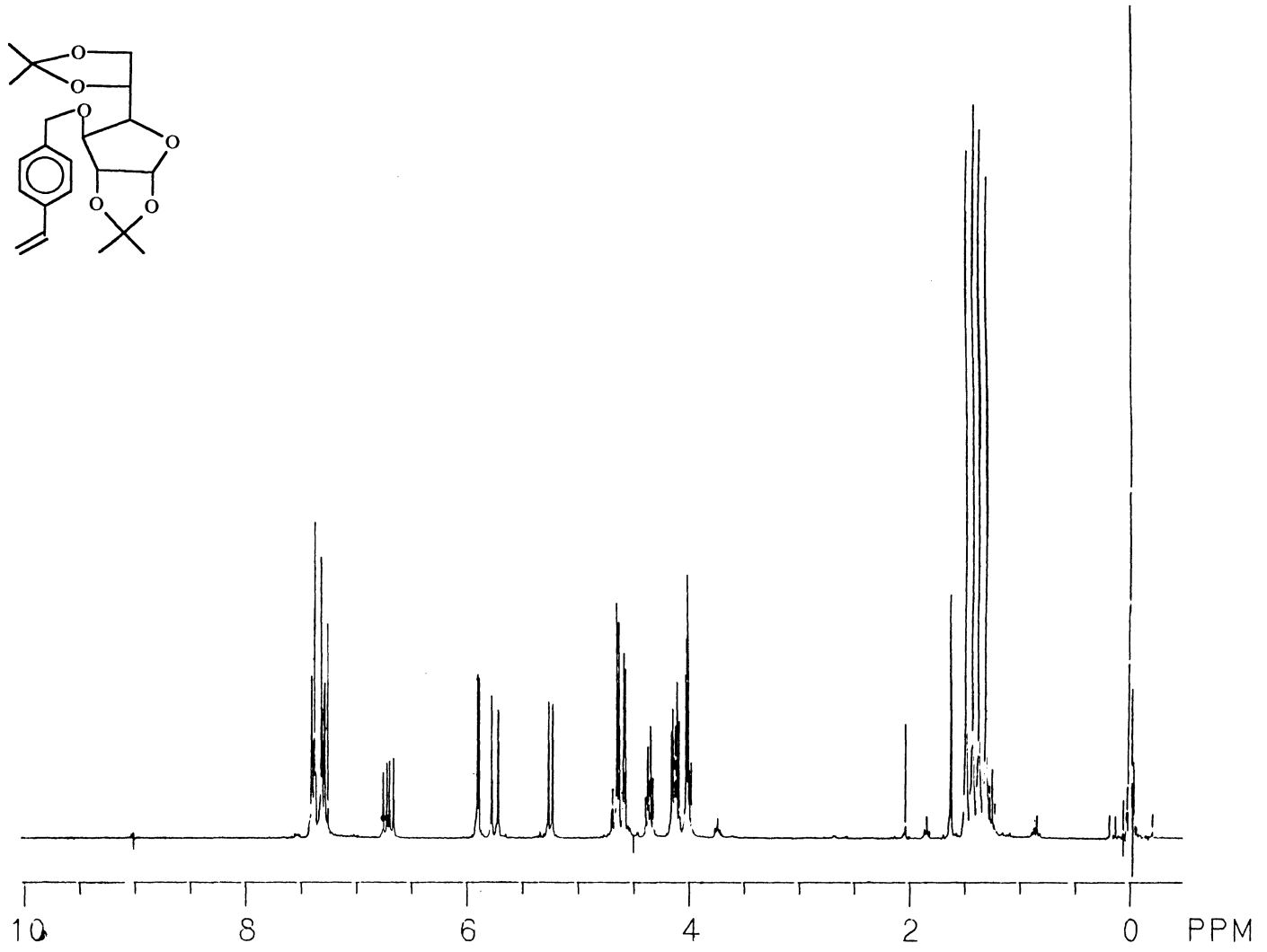

Figure 18: ^{1}H NMR Spectrum of 3-O-Vinylbenzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (13) (meta, para mixture)

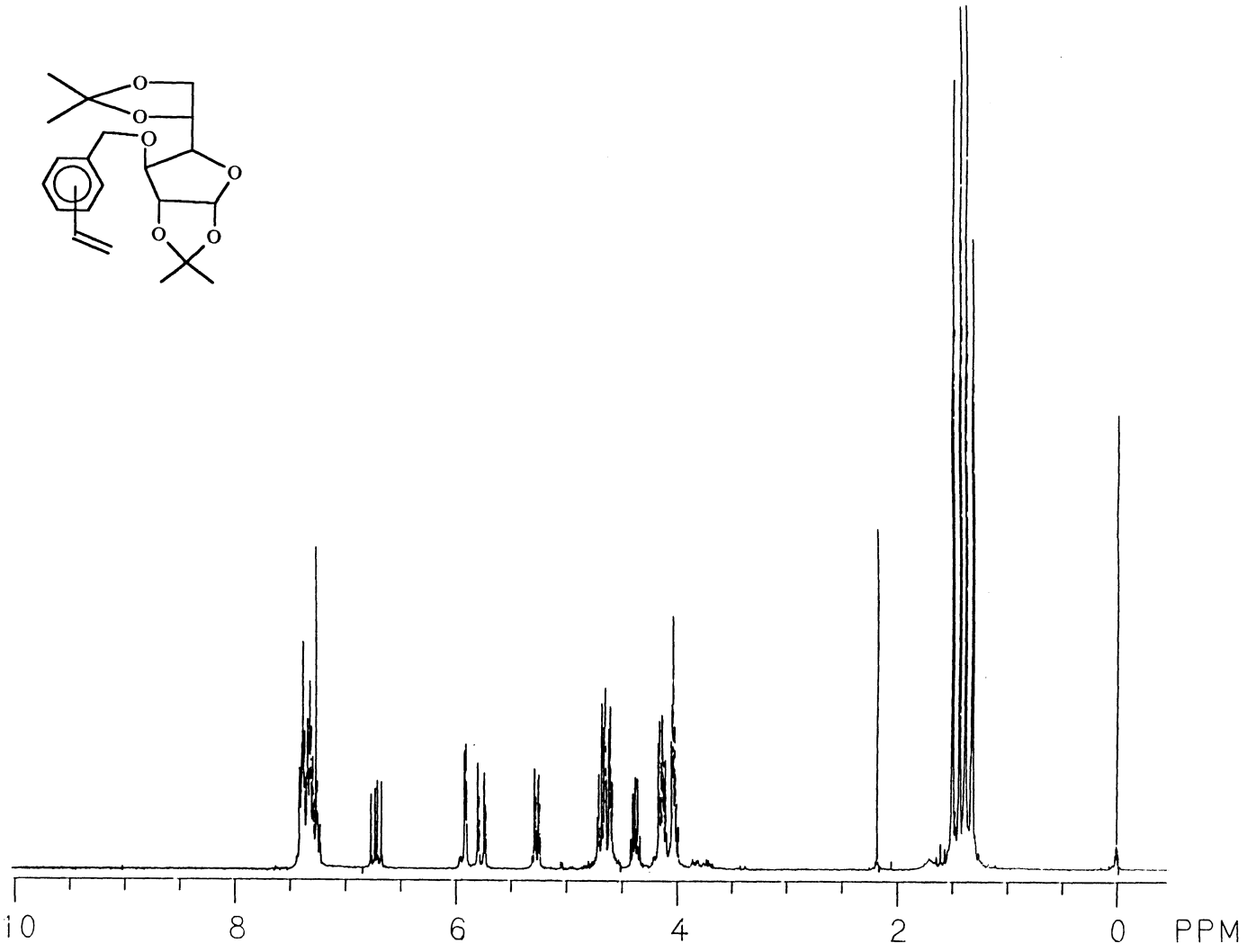

Figure 19: Expanded ^{1}H NMR Spectrum of 3-O-Vinylbenzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (13) (meta, para mixture)

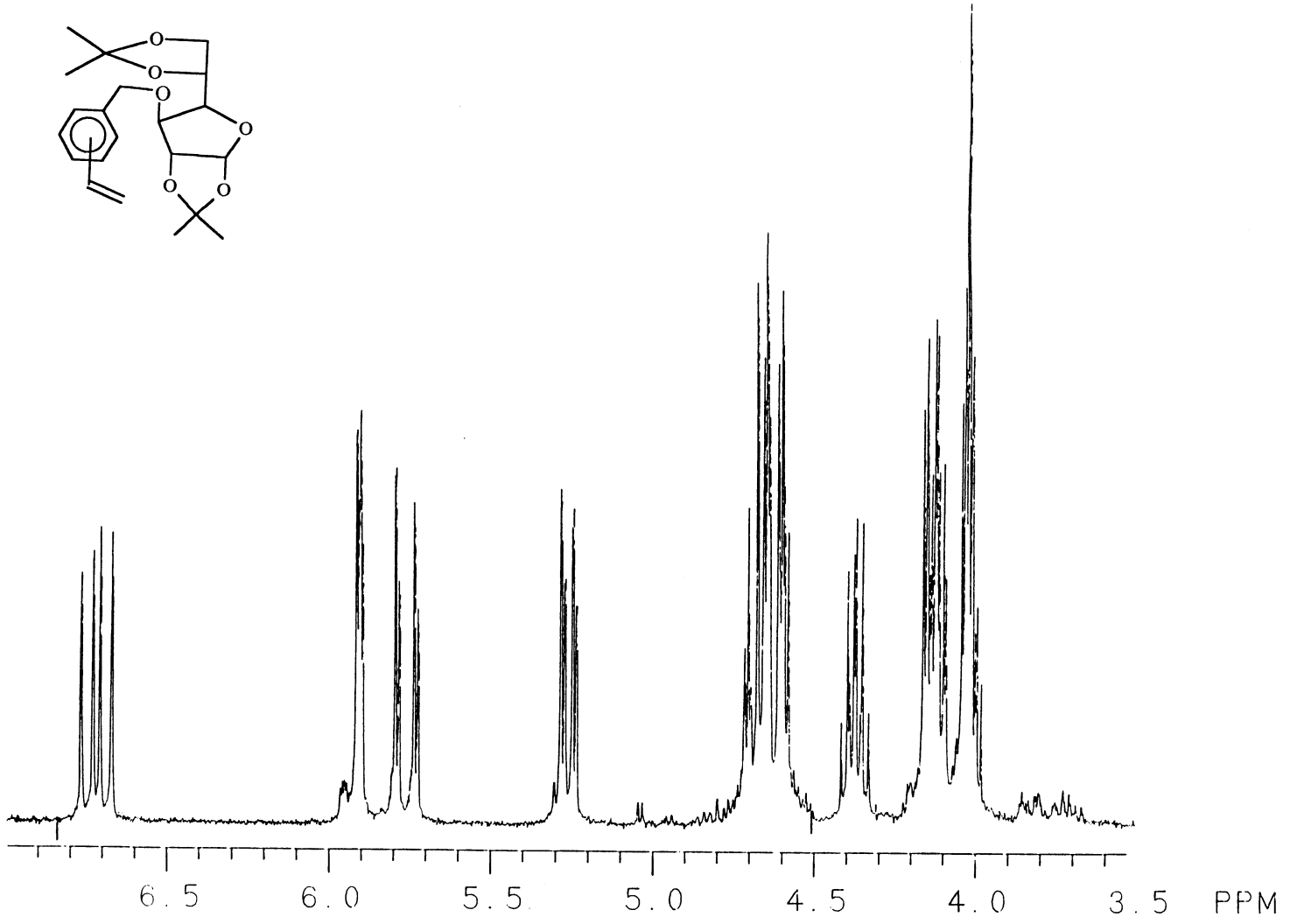

Figure 20: IR Spectrum of 3-O-(p-Vinylbenzyl)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside(13)

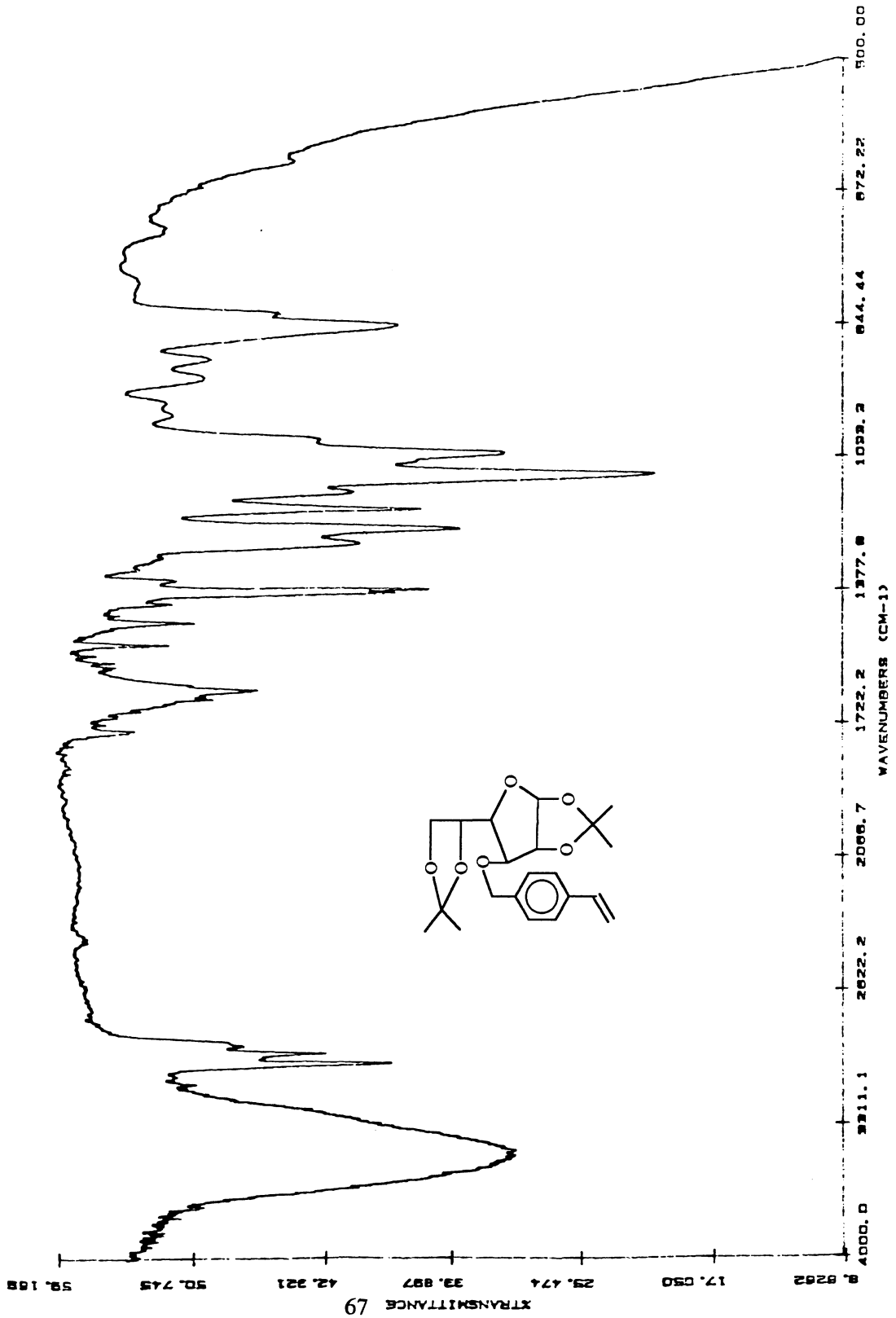

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Figure 21: ^{1}H NMR Spectrum of 3-O-Benzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (15)

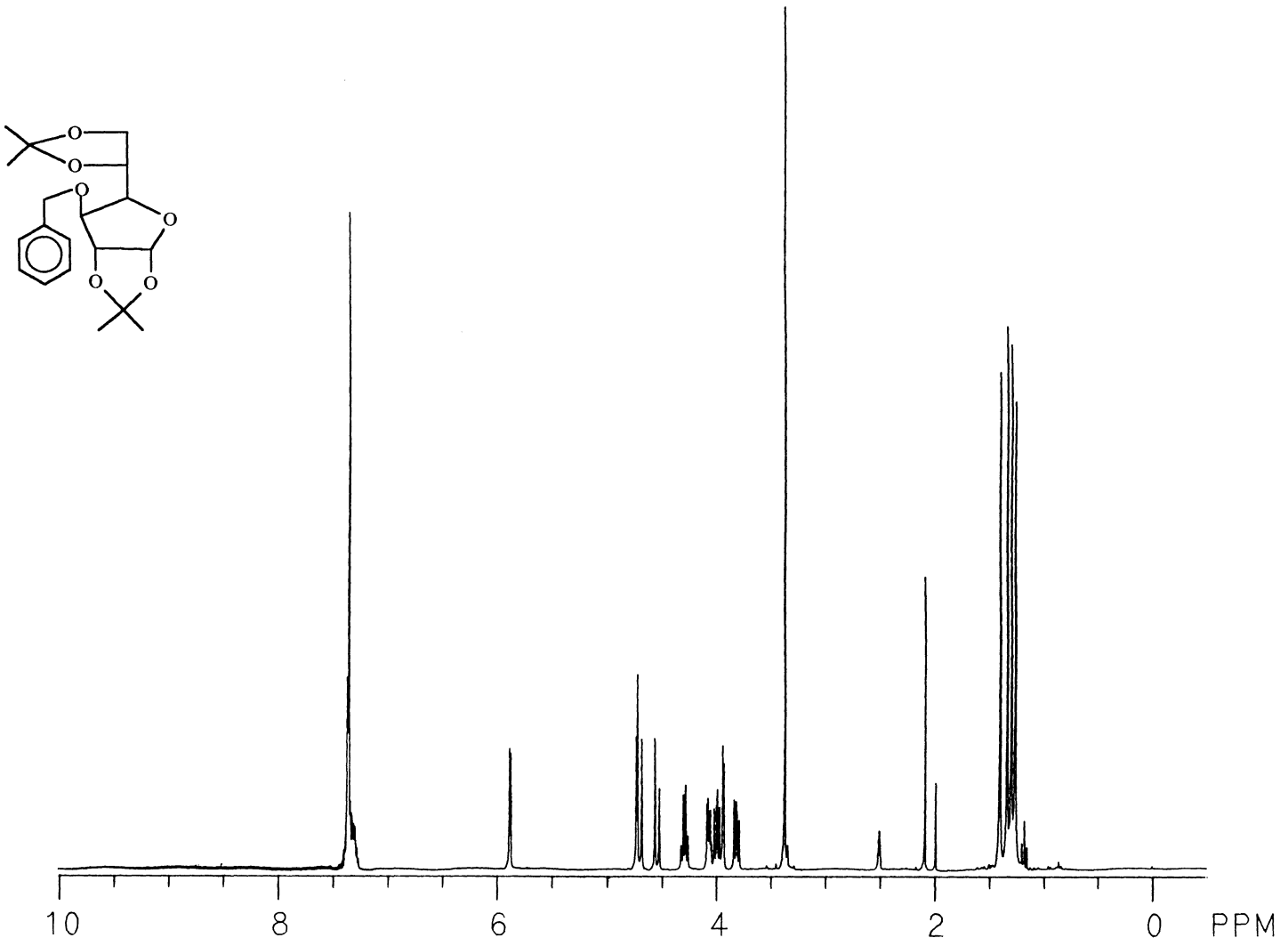


Figure 22: IR Spectrum of 3-O-Benzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranoside (15)

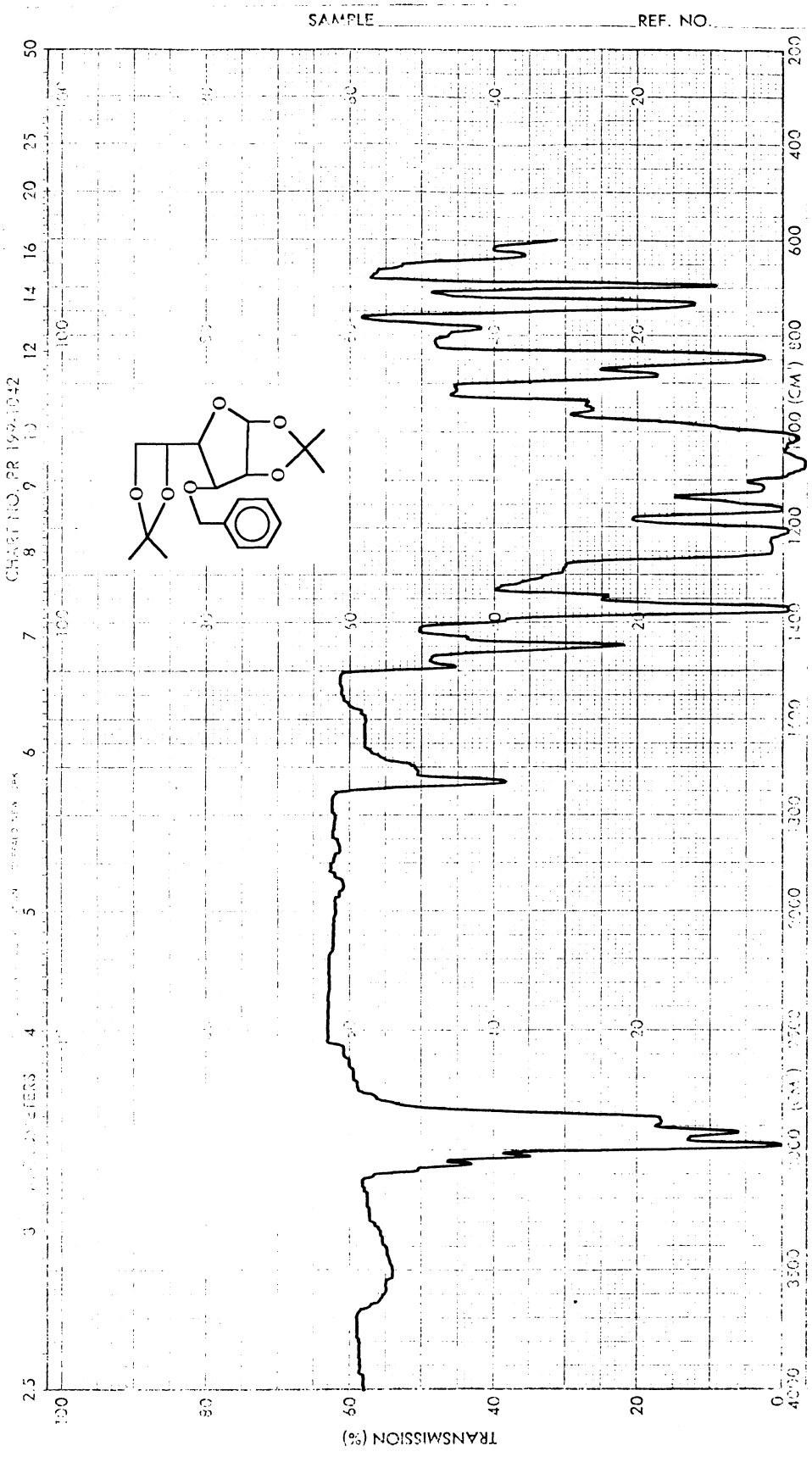


Figure 23: ^{1}H NMR Spectrum of 3-O-Benzyl-1,2-O-isopropylidene-α-D-glucofuranoside (17)

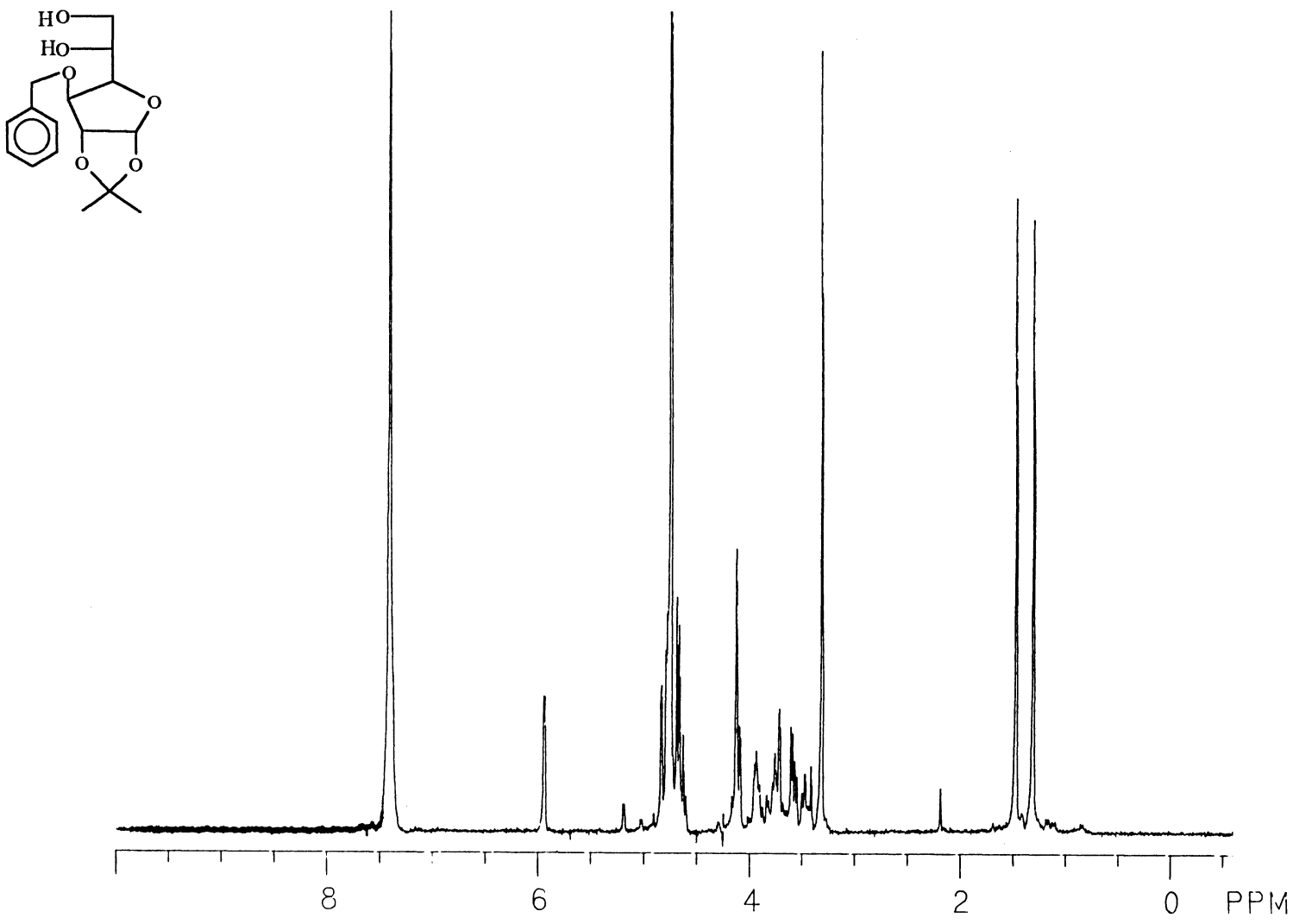
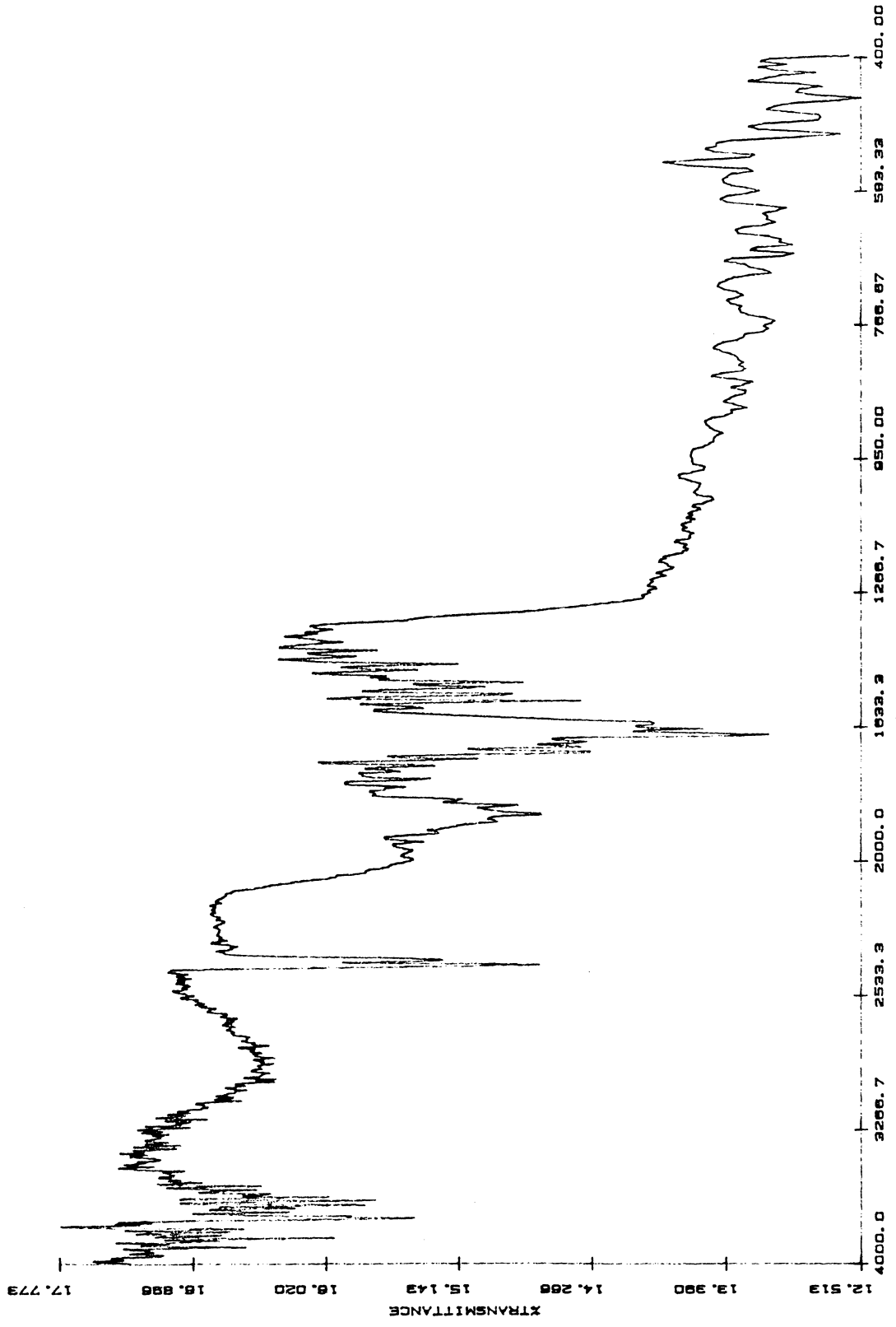


Figure 24: IR Spectrum of Unmodified Silica



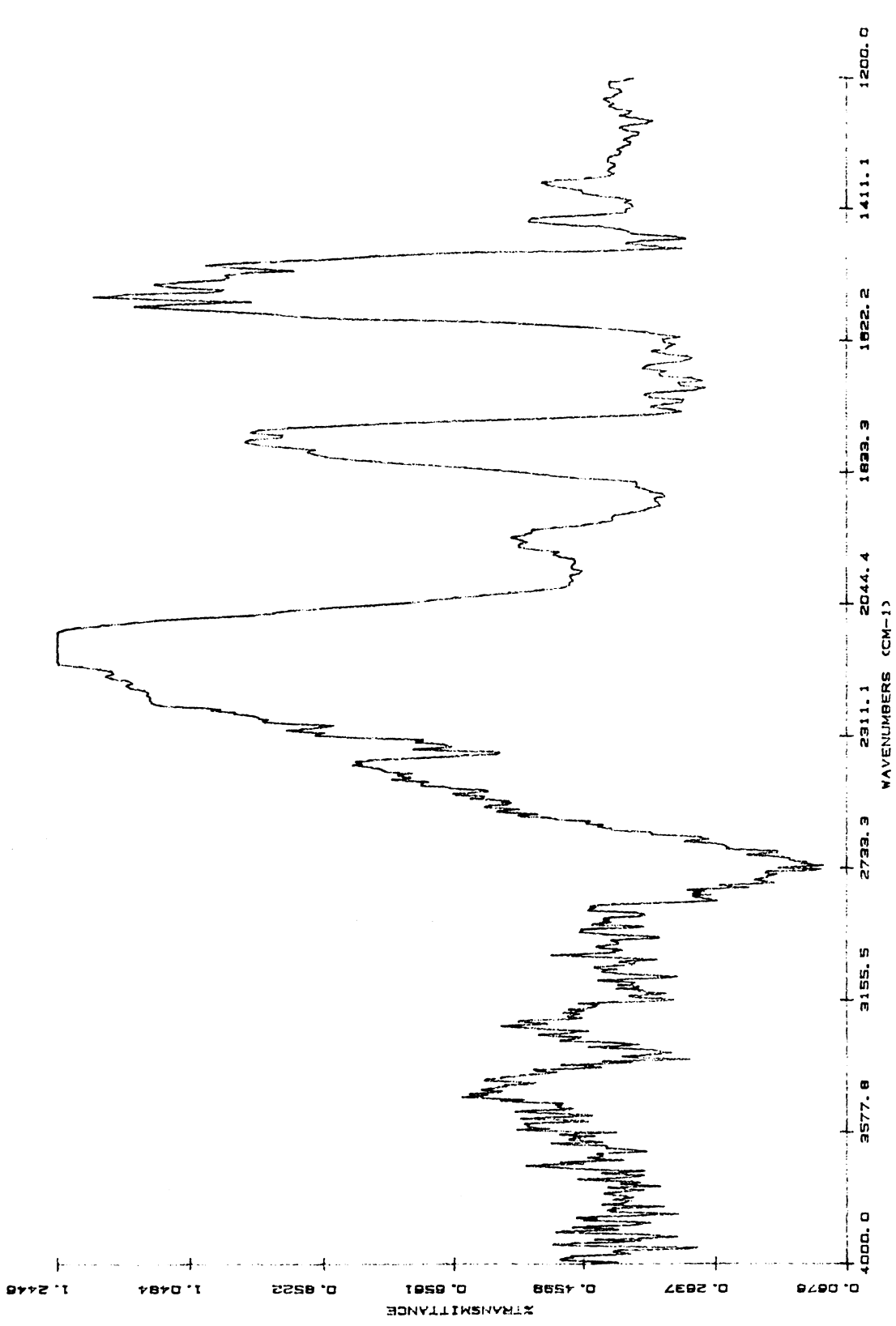


Figure 25: IR Spectrum of Modified Silica

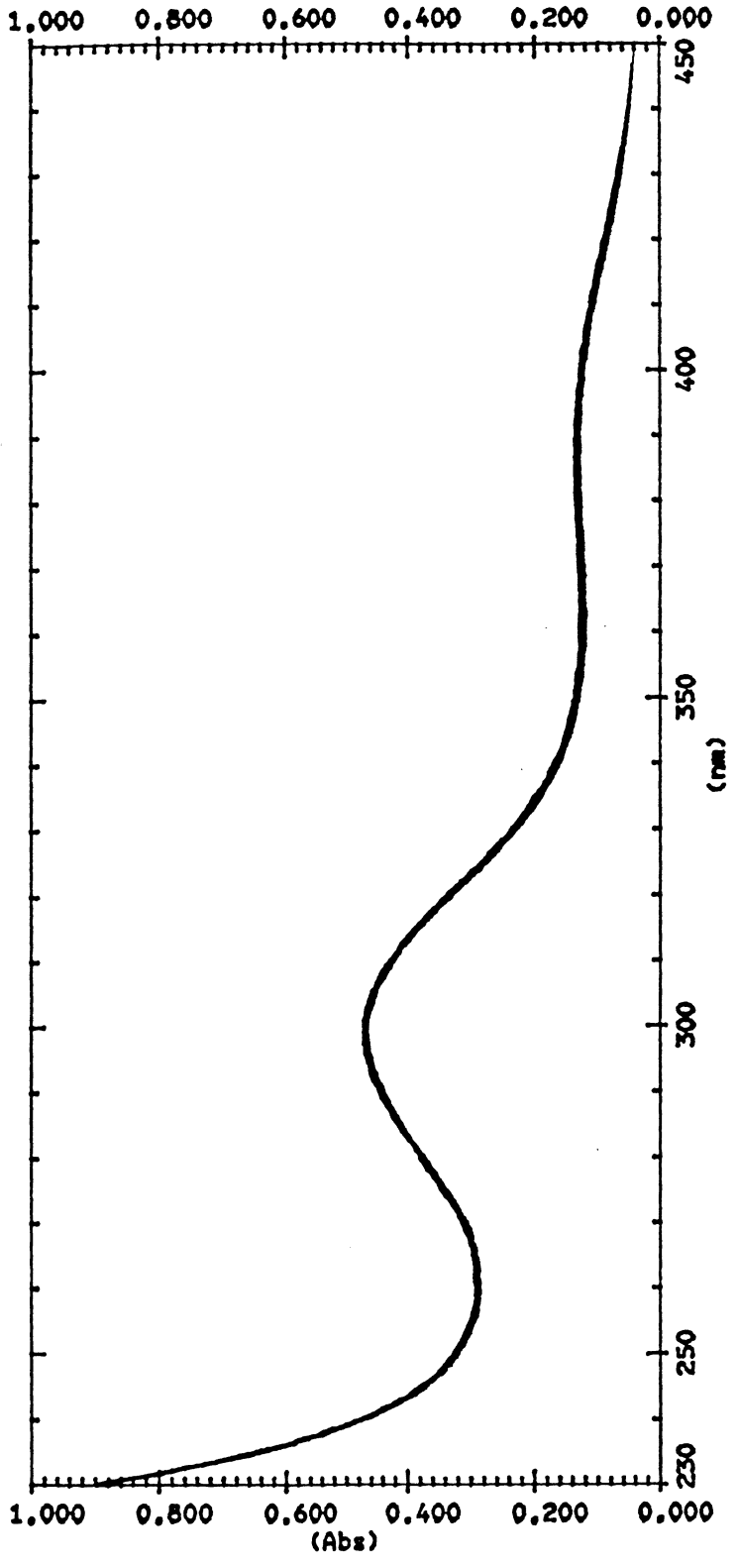


Figure 26: UV Spectrum of Polymer Hydrolysis Solution

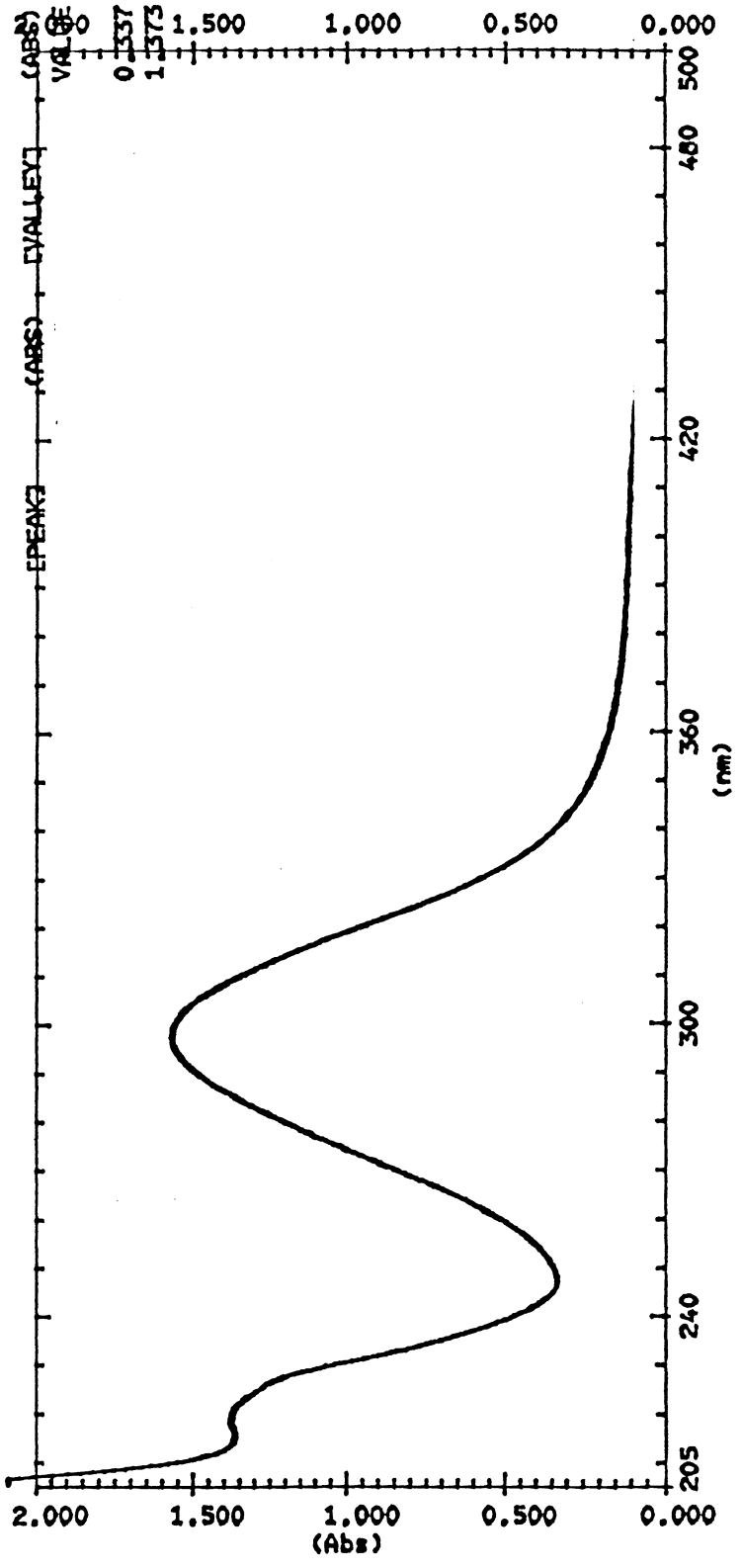


Figure 27: UV Spectrum of 4-Nitrophenyl-α-D-glucopyranoside (Template Molecule)

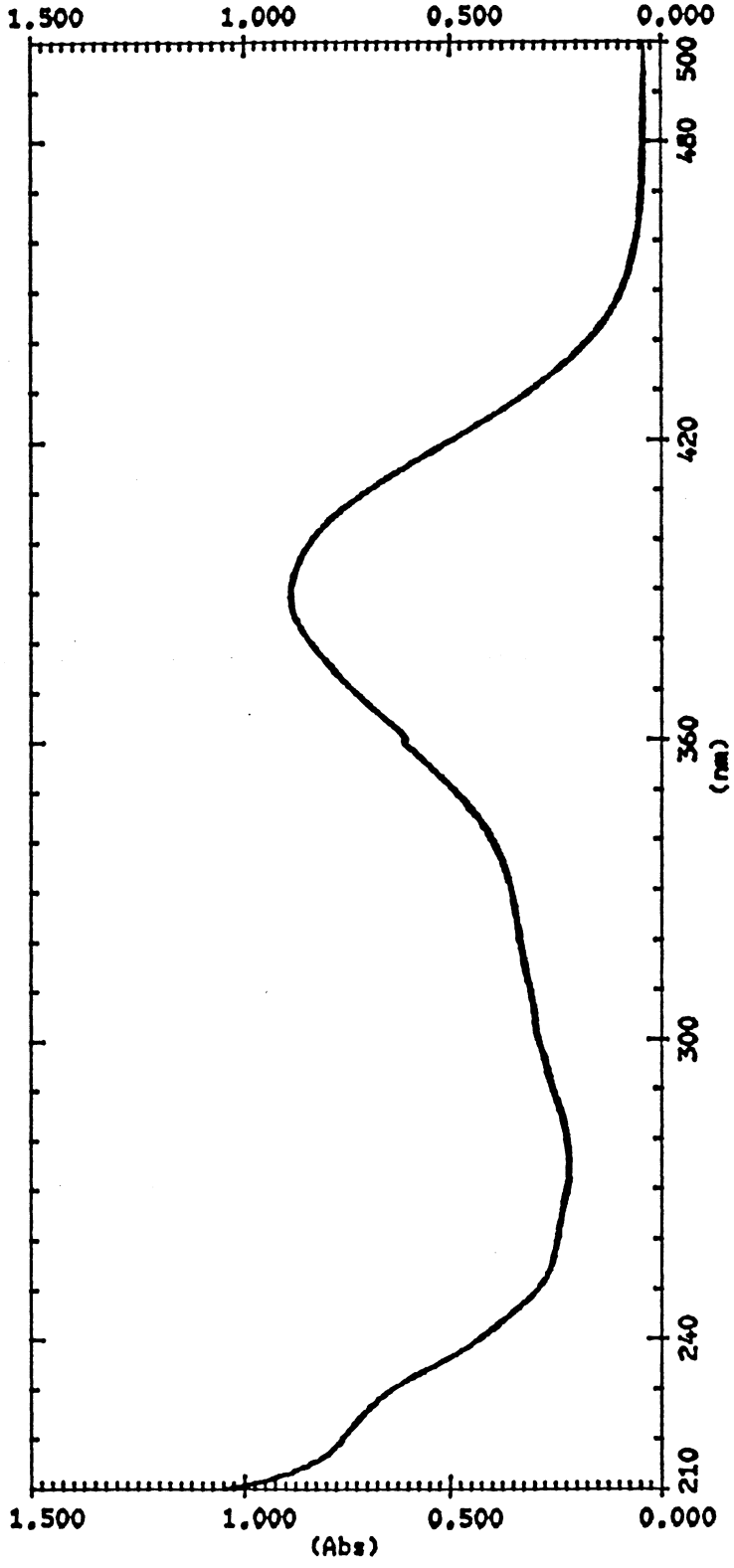


Figure 28: UV Spectrum of potassium salts of 4-Nitrophenol.